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PRINCIPLES

of

PHARMACY

By

HENRY V. ARNY, Ph.M., Ph.D.

Dean and Professor of Chemistry in the College of Pharmacy of Columbia University; Sometime Dean and Professor of Pharmacy in the School of Pharmacy of Western Reserve University; Member of the Committee of Revision of the United States Pharmacopœia, Eleventh Revision; Member of the Committee of Revision of the National Formulary, Sixth Edition

With the Collaboration of

ROBERT P. FISCHELIS, B.Sc., Ph.M., Phar.D

Secretary and Chief Chemist, Board of Pharmacy, State of New Jersey; Sometime Dean and Professor of Pharmacy, New Jersey College of Pharmacy; Special Lecturer, Philadelphia College of Pharmacy and Science

FOURTH EDITION, RESET
WITH 298 ILLUSTRATIONS

PHILADELPHIA AND LONDON
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PHILADELPHIA

PREFACE TO THE FOURTH EDITION

It is now twenty-seven years since the first edition of this book was issued. The three editions published since 1909 have been the personal work of the author and this fourth edition largely represents the labor of the original writer. However, in this edition, it became necessary to secure aid and the undersigned was fortunate enough to secure as collaborator Dr. Robert P. Fischelis of Trenton, N. J., a valued friend and fellow worker of over twenty years standing. Dr. Fischelis has rewritten Chapters I and LII of this edition, has carried out most of the checking necessary in revising U.S.P. and N.F. data and has been responsible for most of the proof-reading and the preparation of the Index. It is our hope that he will be able to carry forward future editions of the book when the senior author becomes inactive.

This fourth edition is based upon the new editions of the United States Pharmacopœia (U.S.P. XI) and the National Formulary (N.F. VI). It affords the student concise information concerning our National Standards and includes in its scope the newest and most useful knowledge of all types of drugs, medicines and chemicals of today. The most recent advancements in medication, notably synthetic chemicals and endocrine preparations, are given particular attention.

The first three editions of this book have been so successful, that it is the earnest hope that this fourth edition will meet with equally friendly reception on the part of the pharmacists and physicians of America.

H. V. Arny.

New York City.

PREFACE TO THE FIRST EDITION

THE subject of pharmacy as understood by the writer consists of the practical application of the sciences of physics and chemistry to medicines and their preparations, as well as sufficient botany to appreciate the character of those vegetable drugs entering into pharmaceutical preparations. As far as botany is concerned, the application of that science to medicine consists in that distinct study, materia medica, but of greater difficulty is an attempt to study the pharmacy of chemicals, both inorganic and organic, without at least some explanation of the principles underlying the science of chemistry. This explains the brief Introductory Chapters to Parts III and IV, which students have found of value as an adjunct to their instruction in pure chemistry.

While not desiring to hamper instruction by artificial limitations, the entire subject of pharmacy is so vast that some gleaning of essentials from those substances of minor importance appeals to the teacher as imperative, and we are fortunate in having a means of elimination in the use of our national standard, the United States Pharmacopœia. Of course no pharmaceutical instruction would prove sufficient were all unofficial drugs excluded, but the existence of a pharmacopœia makes it possible to use that work as the basis of instruction, and in drilling the student in official substances ample opportunity is afforded to refer to those unofficials suggested by the pharmacopœial preparation under consideration.

The book consists of seven* parts:

Part I deals with pharmaceutical processes and a striking feature is the discussion of the arithmetic of pharmacy.

Part II deals with the galenical preparations of the pharmacopœia and those unofficials worthy of notice. It will be noticed that; wherever possible, these preparations are grouped around a typical pharmacopœial recipe, thus avoiding repetition.

Part III deals with the inorganic chemicals used in pharmacy, has an introductory chapter on chemical theories, and discusses chemical arithmetic very fully.

Part IV discusses the organic chemicals used in pharmacy, and that according to the most modern classification. Like Part III, it begins with an introductory chapter on the theory of the class of chemicals discussed.

Part V is devoted to chemical testing, and summarizes the analytic methods of the Pharmacopœia.

Part VI takes up the prescription from the time it is written to the time it is dispensed.

Part VII* gives the laboratory work which has been followed with much success by students of the writer. A notable feature of this part is the exercise in equation writing and in chemical arithmetic that the work affords.

H. V. ARNY.

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* The matter in Part VII of the former editions has been in the present 1937 edition distributed among the chapters where the preparation in question is given formal consideration.

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LIST OF ABBREVIATIONS

A. = *Annalen der Chemie und Pharmacie.*
A. J. P. = *American Journal of Pharmacy.*
A. Ph. A. = *Proceedings of the American Pharmaceutical Association.*
Am. Ch. Jl. = *American Chemical Journal.*
Am. Dr. = *American Druggist and Pharmaceutical Record.*
Am. Jl. Physiol. = *American Journal of Physiology.*
Analyst = *The Analyst.*
Ann. chim. phys. = *Annales de chimie et de physique.*
Ann. Phil. = *Annals of Philosophy.*
Apoth. Zt. = *Apotheker Zeitung.*
Arch. d. Pharm. = *Archiv der Pharmazie.*
B. = *Berichte der deutschen Chemischen Gesellschaft.*
Ber. d. Pharm. Ges. = *Berichte der deutschen Pharmazeutischen Gesellschaft.*
Bull. Assoc. chim. suc. dist. = *Bulletin de l'Association des chimistes de sucrerie et de distillerie.*
Bull. Pharm. = *Bulletin of Pharmacy.*
Bull. sci. pharmacol. = *Bulletin des sciences pharmacologiques.*
C. A. = *Chemical Abstracts.*
Can. Ph. Jl. = *Canadian Pharmaceutical Journal.*
Ch. & Dr. = *The Chemist and Druggist.*
Ch. Cent. = *Chemisches Centralblatt.*
Ch. Eng. = *The Chemical Engineer.*
Ch. Ind. = *Chemistry and Industry.*
Ch. News = *The Chemical News.*
Ch. Rev. = *Chemical Reviews.*
Ch. Zt. = *Chemiker-Zeitung.*
Ch. Zt. Rep. = *Chemisch-technisches Repertorium.. Beilage zur Chemiker-Zeitung.*
Comp. rend. = *Comptes rendus des séances de l'Academie des sciences.*
D. A. Ap. Zt. = *Deutsch-amerikanische Apotheker-Zeitung.*
Dingl. = *Dingler's Polytechnisches Journal.*
Dr. Bull. = *Druggist's Bulletin.*
Dr. Circ. = *The Druggists' Circular.*
8th Int. Cong. App. Ch. = *Proceedings of the Eighth International Congress of Applied Chemistry.*
Elect. World = *The Electrical World.*
Eng. Min. Jl. = *The Engineering and Mining Journal.*
F. I. D. = *Food Inspection Decisions, Bureau of Chemistry, U. S. Department of Agriculture.*
Helv. Ch. Acta = *Helvetica Chimica Acta.*
Ind. Ch. = *The Industrial Chemist.*
J. B. = *Jahresbericht über die Fortschritte der Chemie und verwandter Teile anderer Wissenschaften.*
Jl. A. M. A. = *The Journal of the American Medical Association.*
Jl. Am. Ch. Soc. = *The Journal of the American Chemical Society.*
Jl. A. Ph. A. = *The Journal of the American Pharmaceutical Association.*
Jl. A. O. A. C. = *Journal of the Association of Official Agricultural Chemists.*
Jl. Ch. Ed. = *Journal of Chemical Education.*
Jl. Ch. Soc. = *The Journal of the Chemical Society.*
Jl. de. ph. = *Journal de pharmacie.*
Jl. de ph. et ch. = *Journal de pharmacie et de chimie.*
Jl. Exp. Med. = *Journal of Experimental Medicine.*
Jl. Frank. Inst. = *Journal of the Franklin Institute.*
Jl. Ind. Eng. Ch. = *The Journal of Industrial and Engineering Chemistry.*
Jl. Phys. Ch. = *The Journal of Physical Chemistry.*

Jl. Physiol. = *Journal of Physiology.*
Jl. prakt. Ch. = *Journal für praktische Chemie.*
Jl. Soc. Ch. Ind. = *Journal of the Society of Chemical Industry.*
Merck's Rep. = *Merck's Report.*
Met. Ch. Eng. = *Metallurgical and Chemical Engineering.*
Meyer Bros. Drug. = *Meyer Brothers' Druggist.*
N. J. Ph. A. = *Proceedings of the New Jersey Pharmaceutical Association.*
N. R. = *New Remedies.*
Nat. Dr. = *The National Druggist.*
N. W. Dr. = *The North-Western Druggist.*
Perf. Ess. Oil Rec. = *Perfumery and Essential Oil Record.*
Ph. Acta Helv. = *Pharmaceutica Acta Helvetiæ.*
Ph. Arch. = *Pharmaceutical Archives.*
Ph. Era = *Pharmaceutical Era.*
Ph. Jl. = *The Pharmaceutical Journal and Pharmacist.*
Ph. Post. = *Pharmaceutische Post.*
Ph. Rec. = *The Pharmaceutical Record.*
Ph. Rev. = *Pharmaceutical Review.*
Ph. Rund. = *Pharmaceutische Rundschau.*
Ph. Weekbl. = *Pharmaceutisch Weekblad.*
Ph. Zent. = *Pharmaceutische Zentralhalle.*
Ph. Zt. = *Pharmazeutische Zeitung.*
Pharm. Era = *The Pharmaceutical Era.*
Phil. Trans. = *Philosophical Transactions of the Royal Society of London.*
Phys. Rev. = *Physical Review.*
Pract. Dr. = *The Practical Druggist.*
Proc. Am. Phil. Soc. = *Proceedings of the American Philosophical Society.*
Proc. Ch. Soc. = *Proceedings of the Chemical Society.*
Quart. Jl. Ph. = *Quarterly Journal of Pharmacy.*
Rep. Lab. A. M. A. = *Reports of the Chemical Laboratory of the American Medical Association.*
Repert. Pharm. = *Repertorium für die Pharmacie; von J. A. Buchner.*
Rev. chem. ind. = *Revue de chemie industrielle.*
Rev. gén. sci. = *Revue générales des sciences pures et appliquées.*
Schimmel's Rep. = *Semi-annual Reports of Schimmel & Co.*
Schw. Apoth. Zt. = *Schweizerische Apotheker Zeitung.*
Sch. Wsch. Ch. Ph. = *Schweizerische Wochenschrift fur Chemie und Pharmacie.*
Schweigger's Jl. = *Journal fur Chemie und Physik; hrsg. von S. C. Schweigger.*
Scient. Month. = *Scientific Monthly.*
So. Ph. Jl. = *Southern Pharmaceutical Journal.*
West. Dr. = *The Western Druggist.*
Yearbook A. Ph. A. = *Yearbook of the American Pharmaceutical Association.*
Yearbook Pharm. = *Yearbook of Pharmacy; with the Transactions of the British Pharmaceutical Conference.*
Zt. analyt. Ch. = *Zeitschrift für analytische Chemie.*
Zt. angew. Ch. = *Zeitschrift fur angewandte Chemie.*
Zt. anorg. Ch. = *Zeitschrift fur anorganische Chemie.*
Zt. Biol. = *Zeitschrift für Biologie.*
Zt. Chem. = *Zeitschrift fur Chemie.*
Zt. Elektrochem. = *Zeitschrift fur Elektrochemie und angewandte physikalische Chemie.*
Zt. Phys. = *Zeitschrift für Physik.*
Zt. physiol. Ch. = *Zeitschrift fur physiologische Chemie (Hoppe-Seyler's).*

LIST OF REFERENCE BOOKS

Wootton. Chronicles of Pharmacy. 1910.
Schelenz. Geschichte der Pharmazie. 1904.
J. Q. Adams. Report on Weights and Measures. 1821.
Dayton Miller. Laboratory Physics. 1903.
Hager. Handbuch der pharmaceutischen Praxis. 1913.
Dornke and Reimerdes. Handbuch der Araometrie. 1912.
Tate and Gabb. Alcoholometry. 1930.
Lavoisier-Kerr. Elements of Chemistry. 1806.
Wright. Electric Furnaces. 1905.
Ganot-Atkinson. Physics. 1910.
Parry. The Steam Engine. 1906.
Wilson. Steam Boilers. 1902.
Hausbrand-Wright-Heastie. Evaporating, Cooling and Condensing Apparatus. 1929.
Seidell. Solubilities of Inorganic and Organic Substances. 1919.
Durrans. Solvents. 1931.
Bryden-Dickey. Filtration. 1924.
Bayley. Elemental Crystallography. 1910.
Duncan. Chemistry of Commerce. 1907.
Shoemaker. The Oleates. 1885.
Wiley. Pharmacal Jurisprudence. 1889.
Witte. Essentials in Therapeutics. 1902.
Planten. The Art of Capsulating. 1909.
Renodæus. Dispensatorium. 1631.
Wood. Tablet Making. 1906.
Hollemann-Cooper. Inorganic Chemistry. 1921.
Davis. Advance of Science. 1934.
Getman. Outlines of Theoretical Chemistry. 1922.
Deming. General Chemistry. 1935.
Caven and Lander. Systematic Inorganic Chemistry. 1931.
Sadtler & Coblentz. Pharmaceutical Chemistry. 1906.
Meyer-McGowan. History of Chemistry. 1906.
Thomson. Corpuscular Theory of Matter. 1907.
L. Meyer. Modern Theories of Chemistry. 1888.
Ostwald. Grundriss der Kolloid Chemie. 1907.
Findlay. The Phase Rule. 1923.
Alexander Smith. Inorganic Chemistry. 1918.
Alexander Smith. General Chemistry. 1917.
Krantz. Pharmaceutical Chemistry. 1928.
Partington. Inorganic Chemistry. 1930.
Gmelin-Kraut. Handbuch der Anorganischen Chemie 1912.
Thorpe. Dictionary of Applied Chemistry. 1913.
Lewis. Valence and Structure of Atoms. 1923.
Haas. Quantum Chemistry. 1930.
Frey. Electronic Conception of Valence. 1921.
Andrade. Structure of the Atom. 1923.
Martin. Industrial Inorganic Chemistry. 1917.
Berliner. Potash Bibliography. 1930.
Lowy and Harrow. Introduction to Organic Chemistry. 1936.
Hopkins. The Rarer Metals. 1923.
Lunge. Sulphuric Acid and Alkali. 1880.
Abegg. Handbuch der Anorganischen Chemie. 1913.
Kopp. Beitrag zur Geschichte der Chemie. 1869.
Beilstein. Handbuch der Organischen Chemie. 1906.
Hill and Kelley. Organic Chemistry. 1932.
Allen. Commercial Organic Analysis. 1923.

Burroughs. Bibliography of Petroleum, U. S. Bureau of Mines Bull. 216 and 220. 1919.
Day. Handbook of the Petroleum Industry. 1922.
Sadtler. Industrial Organic Chemistry. 1923.
Kraemer. Applied and Economic Botany. 1914.
Rusby. Manual of Structural and Descriptive Botany. 1920.
Sayre. Organic Materia Medica. 1917.
Tschirch. Handbuch der Pharmacognosie. 1921.
Armstrong. Carbohydrates and Glucosides. 1912.
Branfoot. Pectic Substances in Plants. 1929.
Haworth. Constitution of Sugars. 1929.
Brown and Crawford. Nitrocellulose Lacquer. 1928.
Lewkowitsch. Oils and Fats. 1922.
Schultz-Julius-Green. Systematic Survey of the Organic Colouring Matters. 1904.
Heusler-Pond. The Terpenes. 1904.
Gildemeister-Kremers. Volatile Oils. 1916.
Parry. Essential Oils. 1919.
Brooks. Non-benzenoid Hydrocarbons. 1922.
Charabot. Huiles Essentielles. 1899.
Wallach. Terpene and Camphor. 1914.
Martin. Perfumes, Essentials Oils and Fruit Essences. 1921.
Gattefosse. Agenda de Chimiste-Parfumeur. 1918.
Piesse. The Art of Perfumery. 1879.
Sornet. Parfums Synthetiques. 1923.
Atkinson. Perfumes and Cosmetics, Their Preparation and Manufacture. 1915.
Mann-Winter. Die Moderne Parfumerie. 1932.
Chilson. Modern Cosmetics. 1934.
Durvelle. The Preparation of Perfumes and Cosmetics. 1923.
Poucher. Perfumes, Cosmetics and Soaps. 1929.
Tschirch. Die Harze and Die Harzbehalter. 1906.
Dupy. Alcaloides. 1887.
Winterstein and Trier. Die Alkaloide. 1910.
Pictet-Biddle. Vegetable Alkaloids. 1913.
Small and Lutz. Chemistry of the Opium Alkaloids. 1932.
Hawk. Physiological Chemistry. 1923.
Czapek. Biochemie der Pflanzen. 1913.
Mann-Cohnheim. Chemistry of the Proteids. 1906.
Plimmer. The Proteins. 1921.
Osborne. The Vegetable Proteins. 1916.
Mendel and co-workers. The Vitamins. 1932.
Medical Research Council (England). The Vitamins; a Survey of Present Knowledge. 1932.
Mangin-Sternberg. Bacteria. 1884.
Hiss and Zinnser. Text Book of Bacteriology. 1917.
Stieglitz. Qualitative Chemical Analysis. 1920.
Jenkins and Du Mez. Quantitative Pharmaceutical Chemistry. 1931.
Munch. Bio-Assays. 1931.
Sayre and Havenhill. Pharmaceutical Latin. 1917.
Sturmer. Pharmaceutical Latin. 1924.
Dorfman. Pharmaceutical Latin. 1936.
Ruddiman. Incompatibilities in Prescriptions. 1910.
Scoville. Art of Compounding. 1914.
Rosenthaler. Grundlagen der Rezeptur. 1930.
Anon. Art of Dispensing. 1915.

PRINCIPLES OF PHARMACY

PART I

THE DEVELOPMENT OF PHARMACY AND PHARMACEUTIC OPERATIONS AND APPLIANCES

CHAPTER I

THE DEVELOPMENT OF PHARMACY

Introduction.—The daily use of drugs and medicines in the treatment of disease down through the ages has brought about the development of a profession as well as an industry devoted to supplying medicines in the most effective forms for administration to the sick.

It is a far cry from the priests of Isis who dispensed prescriptions ordered by the physician-priests of ancient Egypt, to the American pharmacist who compounds prescriptions in his corner drug store upon the written order of the American doctor.

The advances of modern science and commerce have robbed the abode of the pharmacist of much of its ancient glamor and mysticism, but the art of the apothecary is still a requisite of first importance in the preparation of the materials of medicine for safe and effective use.

Origins.—To understand the profession of pharmacy one must glance at the history of the calling whose beginnings, according to Charters, are "lost in the mists of antiquity." References to the apothecary and his art go back to the dawn of recorded history. That the art of preparing medicines and the action of medicines should have been steeped in mystery is not remarkable, if one can imagine our early ancestors face to face with disease, and without knowledge as to its cause or methods and materials to overcome it. The mysteriousness of the disease process led to superstitions in which evil spirits played an important part. These evil spirits could be appeased only by prayer and incantations according to the savage mind.

The spiritual method of approach to disease and its treatment gave way to a more material system, due partly to chance, and possibly to the observation of animals. Having found that most substances which produced some reaction in the body had a bitter or disagreeable taste, it is not surprising that the untutored savage came to regard any such substances as beneficial. This gave rise to a host of materials used in medicine which had little, if anything, to recommend them outside of their bad odor and taste.

At a later period of the Middle Ages, efforts were made to combine the spiritual and the material treatment. It was thought that the Deity alone could cure disease, but that the material remedies had been given to man, and that a certain seal had been put upon these remedies by which man might know them. Thus arose in due time what is known as the doctrine of "Signatures." This is illustrated in the use of the celebrated ginseng root of China, which, like that of the mandrake (Genesis xxx: 14–16), owed its employment to the fact that the root often divides into branches resembling the arms and legs of a man, and this resemblance gave rise to the belief that it conferred strength and virility. The same belief is shown in the names applied to many drug plants, for example, pulmonaria, scrophularia, liverwort, lungwort, bloodroot, etc. The astrological belief that plants, animals, and minerals are under the influence of the planets is shown in the older names of some of the minerals. For example, Saturn for lead, Venus for copper, and Mars for iron. Silver was used in lunacy because it was dedicated to Luna. Physicians to this day head their prescriptions with a sign that originally meant an invocation to Jupiter, but now represents the word "recipe."

Later there developed the alchemists, whose search for the "Philosopher's Stone" and the "Elixir of Life" consumed years of patient but futile effort, as far as turning base metals into gold or discovering a panacea for the ills of humanity are concerned. The by-products of these investigations, however, furnished numerous chemical substances which have been useful both in the arts and in the treatment of disease.

In the original unit of human society, the family, it was the wife and mother who played the rôle of healer. How women were trained to perform their duties as healers is revealed in Ebers' "An Egyptian Princess" of 1550 B. C., and also in Sigrid Undset's "Kristin Lavransdatter" of the thirteenth century A. D. The "pharmakis" of the Greeks, the witches of the Romans, and the wise women of the Germanic tribes are outgrowths of this development.

As the social unit developed into a city, it was the temple that became a sanatorium, and the priests who practiced the healing art. Not only was this true of Egypt, Greece, and Rome, for the modern priests and preachers in sparsely settled countries have been healers of the body as well as of the soul. Egyptian inscriptions indicate that the physician-priests sent their prescriptions to be dispensed by the priests of Isis when, accompanied by the chanter of incantations and spells, they visited the sick. (The Egyptians believed that the medicinal virtues of plants were due to the spirits dwelling within them.) A papyrus of Sent, 3300 B. C., gives directions as to the preparation of prescriptions. In the Ebers papyrus, 1550 B. C., mention is made of blisters, ointments, clysters, mineral and vegetable drugs. About seven hundred drugs are described in this work, at least eighteen of which are listed in the U. S. Pharmacopœia of today.

The art of the apothecary is alluded to very early in Old Testament history, and there are frequent references to materials used as spices and perfume materials which are also used as drugs. However, the word "apothecary" as it appears in the Bible, probably refers to "perfumers" rather than medicine-makers, as there is no clear record of the practice of the art of the apothecary, as such, among the early Hebrews, nor are there references to the administration of internal remedies in Biblical literature.

There are also records to indicate that pharmacy was practiced at a very early period in China. Ching-Hong, a contemporary of Menes I of Egypt, was learned in the art, and made concoctions and extracts of plants.

While many of the drugs used in earliest times have survived and are listed in our modern pharmacopœias, the basis for their use has changed considerably. The scientific basis for the use of drugs, as distinct from any mythological basis, dates back to the time of Hippocrates (460 B. C.). Nearly four hundred drugs are named in his writings, and he directed and employed preparations belonging to the classes of poultices, gargles, pills, ointments, collyria, and inhalations. Dioscorides wrote his great work on Materia Medica in A. D. 77–78, and this still remains the most important work on the plants and drugs used in ancient times, and continued as a recognized authority on the subject for over sixteen hundred years.

Galen (A. D. 131–201), a Greek who later became a Roman citizen, was both a pharmacist and a physician, and originated many of the preparations of vegetable drugs. To this day these preparations are referred to as galenicals. He added about two hundred plant drugs to the list described by Dioscorides.

The lay helper of the ancient priests was considered an irregular practitioner, and was never highly esteemed. However, with the development of Arabian science and pharmaceutic art, the lay physician, as a class, and the lay apothecary came into their own. Bagdad is said to have had the first public apothecary shop. The separation of pharmacy from medicine was recognized in the eighth, and legalized in the eleventh century. This development found its way into Europe along with the Arabian civilization.

The establishments for dispensing medicines at Cordova, Toledo and other large towns under Arab rule, were placed under severe legal restrictions. The first undoubted record of the separation of medicine and pharmacy is found in a decree of Emperor Frederick II of Sicily, who in A. D. 1224, just after the close of the Crusades, issued a law, which remained in force for a long time in the two Sicilies, by which every medical man was required to give information against any pharmacist who should sell bad medicine. The pharmacists were divided into two classes, the "stationarii," who sold simple drugs and nonmagisterial preparations at a tariff determined by competent authorities, and the "confectionarii," whose business it was to dispense scrupulously the prescriptions of medical men; all pharmaceutical establishments were placed under the surveillance of the college of medicine.

In the monastic period, pharmacy was to a great extent under the control of the religious orders, particularly the Benedictines, who, from coming into contact with the Arabian physicians, devoted themselves to pharmacy, pharmacology, and therapeutics; but, as monks were forbidden to shed blood, surgery fell largely into the hands of barbers, so that the class of barber-surgeons came into existence, and the sign of their skill in blood-letting still appears in the form of the barber's pole, representing the application of bandages.

Just as Galen is considered the high priest of the school employing vegetable drugs, so Paracelsus is the outstanding figure in the introduction of chemical salts for the treatment of disease, making use of some of the by-products of the alchemistic era.

The first organized body of pharmacists originated in Bruges, Belgium, in 1297. It was in the nature of a secret society, and possessed a hall, a constitution and by-laws, and an official seal. This was the period in which guilds were very common. Other guilds, or organized bodies of pharmacists, were soon formed in different parts of Europe and were the prototypes of the pharmaceutical organizations of the present day. In England the separation between medicine and pharmacy came somewhat later than on the continent of Europe. The earliest record of an apothecary shop in London dates back to 1345.

Apothecaries.—The early apothecary, working in his shop, was manufacturer, compounder, and dispenser, all in one. There was no division of labor in the modern sense. As a result, many of these apothecaries became earnest research workers, delving into the mysteries of the chemistry of plant drugs in order to determine their active principles. The outstanding names of apothecaries connected with research activities among a host of others, are those of Carl Wilhelm Scheele, a Swedish pharmacist of the eighteenth century, who discovered, among other things, oxygen, chlorine, hydrofluoric and prussic acids and glycerin; Frederick Sertuerner, a German pharmacist, who discovered morphine; Pelletier and Caventou, French pharmacists, who discovered quinine; Davy, who served an apprenticeship in a drug store in his early years and was the first to suggest the use of nitrous oxide gas in anesthesia; Crawford W. Long of Georgia, a pharmacist and physician who made the first actual use of ether as an anesthetic in a surgical operation; and later, John Uri Lloyd, whose work in the early eighties laid the foundation for subsequent researches in colloidal chemistry. Closely associated with pharmacy in his early days was Justus von Liebig who with Friederich Woehler laid the foundation for important discoveries in inorganic and organic chemistry.

Foreign Influence.—In addition to the individual contributions of pharmacists to the art and science of pharmacy, each of the European nations contributed some specific development to the practice of pharmacy. The development of local state pharmacopœias may be traced to the early Italian pharmacist. The development of guilds and the control of the practice of the apothecary's art by them was a special contribution of the French, although other European countries made their contributions to this system. These guilds were abolished by the French Revolution and replaced by the present pharmaceutical societies. The control of pharmaceutical practice by state concession was the particular contribution of Germany, but concessions were granted by the state in many other European countries as well. It is noteworthy that the system of concessions was retained in Germany after the French Revolution, although other callings were made free. The latter-day English system of permitting pharmacies to flourish without much restriction is, perhaps, the forerunner of the American system which has supplied us with a drug store at almost every prominent street corner.

One might have supposed that with the Spanish, French, Dutch, German, and English settlements in America, a practice of pharmacy peculiar to those countries would have sprung up in the various localities which the respective groups colonized. Undoubtedly, pharmacy was practiced among these various settlers as nearly as possible as in the country from which they hailed. At the present time, however, there is little to indicate that the peculiarities of the practice of pharmacy, as exemplified in these countries, have been carried down to the modern American drug store to any great extent. To be sure, one still finds in foreign settlements within the United States the characteristics of the pharmacies which served the settlers in their Mother Countries, and the influence of the German apothecary, the French apothecary and the English apothecary have made themselves felt in the development of the American pharmacist. The average American pharmacy, however, is a characteristic development and does not resemble any particular foreign type of pharmacy, unless it be the English chemist's shop. In a metropolis like New York, one can still find occasional French pharmacies or Spanish pharmacies or a "Deutsche Apotheke," patronized almost exclusively by the natives of the countries represented and always located in a distinctly foreign settlement. The same is true of foreign communities in the various States. Such pharmacies import and supply the drugs peculiar to the country of their origin. In general, however, the drug stores found from coast to coast and from border to border throughout the United States follow a fairly regular pattern, and differ only in the emphasis placed on the various lines of commodities and service provided and the drugs and medicines whose use may be peculiar to the locality.

Contemporary Pharmacy.—Pharmacy as practiced today may be defined as the art and science of collecting, identifying, preparing, preserving, evaluating, compounding, and dispensing drugs and medicines. Giving these terms their broadest interpretation, this definition carries the drug or medicine from its original source to the actual consumer or patient.

In each activity one encounters both a professional and a commercial or business aspect; the pharmacist appears in a dual rôle. Like the physician, surgeon or dentist, he must invest in a technical education, and must equip an "office" in which to work. But he must also invest in a stock of drugs and medicines.

The business aspects of pharmacy involve wholesaling, manufacturing, and retailing. When one speaks of pharmacy and pharmacists, therefore, one must indicate the branch of pharmaceutical work in which the individual is engaged. Retail pharmacists, manufacturing pharmacists, pharmaceutical chemists and wholesale druggists are specialists in the pharmacal profession, just as orthodontists, exodontists, dental surgeons, orthopedists, pediatricians, and laryngologists are specialists in dentistry and in medicine.

Individuals, firms or corporations devoting their time to the collection of pharmaceutical products need not necessarily be pharmacists, although usually at least one pharmacist is connected with every such organization. Collection of drugs requires a knowledge of their sources. The following tabulation will give some idea of the range of sources: (1) *animals:* bacteria and bacterial products (although bacteria are classified as vegetable organisms, serums are obtained from animal sources), insects, organs and parts of organs, glands and parts of glands, tissues, secretions, blood serums; (2) *vegetables:* whole plants, roots, rhizomes, tubers, bulbs, corms, barks, twigs, woods, pith, leaves, hairs, glandular outgrowths, flowers, fruits, seeds, excrescences, cell contents and derivatives; (3) *minerals:* chemical elements, chemical compounds (acids, bases, salts), mixtures of chemical compounds (crude and refined); (4) *synthetics:* chiefly products of the organic chemical laboratories built up from carbon and its compounds.

Skill and expert knowledge are required to select the proper species of medicinal plant; the particular gland or organ from the viscera in the slaughter houses; the proper germ from which cultures are grown in the preparation of serums, vaccines, bacterins, etc.; chemical substances of the proper composition and purity. Legal standards for most of the raw materials and finished products are provided in Federal and State Drug Laws enforced by the Federal Food and Drug Administration, State Food and Drug Bureaus, Boards of Health, Boards of Pharmacy and local Health Departments.

The actual growing and collection of medicinal plants was at one time a part of the normal activity of retail pharmacists. One of the rules laid down for the apothecary in the time of Henry VIII read as follows: "His garden must be at hand, with plenty of herbs and seeds and roots." Some vegetable drugs are cultivated; others grow wild. They are obtained in their native habitats or in the cultivated fields by persons trained in identifying and obtaining the particular part of the plant desired. Producers are usually subsidized by crude drug merchants and their products are handled very much like other farm products.

In the case of animal drugs, the slaughter houses gather the particular organs, glands, tissues, blood, etc. desired and arrange for their sale, usually on contract.

Biological products are produced either by inoculating animals with the disease-producing bacteria or toxins and obtaining the blood serums of such animals after they have become immunized against enormous doses of bacteria or toxins, or by growing the specific disease germs on suitable media, killing or attenuating them and preparing bacterial vaccines.

Crude medicinal chemicals may be mined, or obtained as a result of chemical reactions and special processes. The inorganic chemical industry depends on the air, the mineral resources of land and sea and to some extent on animal and vegetable structures for its sources of raw materials. The organic chemical industry depends largely on laboratory syntheses. The crude and intermediate products used in preparing organic medicinal chemicals are derived largely from coal tar, petroleum, and wood. The constituents of various plant and animal cells or tissues also furnish highly important medicinals such as alkaloids, glucosides, enzymes, and ferments.

World politics, tariffs, and wars, as well as local industrial conditions, therefore, have their effect upon the supply of drugs and medicines as they do upon other commodities. In recent years the chemical industry, both inorganic and organic, has been very closely identified with the supply of medicinal preparations. This is particularly true of the organic chemical industry. The intermediate products which are the sources of medicinal chemicals are also the sources of chemicals used in gas warfare and the manufacture of explosives. The interest of the Government in becoming independent of foreign sources and encouraging the development of a self-contained chemical industry within the United States has had a beneficial influence upon the medicinal chemical industry.

The preparation of drugs and medicines to meet legal and technical standards requires physical, chemical, biological and bacteriological tests for identity, purity and strength. Few retail pharmacists are equipped to make such tests. They rely almost exclusively upon the label statements and guarantees of manufacturers. The manufacturers maintain "control" laboratories where such tests are made on both crude materials and finished preparations. The actual testing is done by specialists who may or may not be pharmacists, but who have, at any rate, specialized in the particular subdivision of scientific pharmacy in which they are engaged.

When the retail pharmacist manufactures the preparations which he dispenses, he must accept full responsibility for their strength and for the truthfulness of the statements which he makes on his labels. When he dispenses the preparations of the manufacturer, he also is held responsible for the quality of the products dispensed, but if the manufacturer is a responsible firm, he may expect the firm to share his responsibility morally, if not legally. There are private commercial laboratories which will test drugs and medicines for small manufacturers and collectors of drugs whose volume of business does not warrant maintaining a laboratory of their own. Government laboratories often test the quality of medicinal preparations supplied to retailers, physicians, and hospitals by purchasing suspected products from various sources, but they do not test medicinal preparations of various manufacturers before they are sent out from these laboratories. The exception to this is the testing of arsphenamine, and of serums, vaccines, and other biological products by the United States Public Health Service before they are released for the market.

Requirements as to the labeling of drugs and medicines are outlined in Federal and State regulations, but evasive statements are frequently made on labels for the purpose of selling substandard products under standard names. This occurs most frequently on highly competitive items when there appears to be a need for shading prices. Reduction in the quantity of active constituents, or substitution of cheaper constituents for the more expensive ones, is sometimes resorted to, and while the changes may be noted on the label, the buyer rarely stops to examine it. The problem of labeling has taxed the ingenuity of legal and technical experts. Large manufacturing houses employ experts to aid them in devising and wording labels, and the U. S. Food and Drug Administration has a Division of Drug Control where label statements are passed upon. It is quite possible for an unscrupulous manufacturer to label his product accurately, but to make claims and statements in the advertizing literature that does not accompany the package, which do not correspond to his label.

The preservation of drugs and medicines after they are manufactured is a problem that has challenged the best minds in the pharmaceutical profession, particularly since adequate methods of testing the efficiency of drugs have been developed. Biological products, such as diphtheria antitoxin and smallpox vaccine, are dated to indicate the length of time for which they may be considered active. This is done because it was established early in the history of the use of these products that they deteriorate upon standing. The development of biological testing methods for vegetable drugs, such as digitalis, ergot, and others, brought forcefully to the attention of physicians and pharmacists that preparations of these drugs also deteriorate with age and that some precaution should be taken to insure the use of an active preparation when it is prescribed. This work has not progressed to the extent of establishing definite periods of time during which such preparations may be considered active and after which they must be destroyed by the pharmacist. However, there are some manufacturers who place a date of test or a date of manufacture on containers of some of these preparations as a warning to physicians and pharmacists regarding possible deterioration. In the meantime, studies are under way to determine causes of deterioration, rapidity of deterioration and methods of reducing deterioration to the minimum by the use of containers which shut out certain light rays, and by providing favorable conditions of storage with reference to temperature, light, and atmospheric conditions.

Commerce in Drugs in Terms of Expenditure by the Public.—Annually, the people of the United States spend approximately $715,000,000 for drugs and medicines, according to a survey made by Korem and Fischelis for the Committee on the Costs of Medical Care. It is estimated that of this total, only 27 per cent ($190,000,000) represents the amount spent for prescriptions, or purchases made with the direct advice of medical practitioners, while $525,000,000 represents the amounts spent by the public for self medication.

Drugs purchased by the public for self medication are of two main types: "home remedies" and "patent medicines." The retail sales of home remedies account for $165,000,000, or 23 per cent of the total drug bill of the United States. Whereas "home remedies" are mostly bought without the express instruction of the medical profession, the general classification includes chiefly nonsecret preparations which are on the whole approved by the family physician, and many of the purchases are doubtless made at the suggestion of medical practitioners. The annual sales of "patent medicines" amount to $360,000,000. The consumption of these products is condemned in no uncertain terms by physicians, as representing a waste of money and a source of actual or potential harm. Thus a total of $525,000,000 is spent by the American people for medicines on their own initiative, to cure minor or chronic ills which seem too trivial or too frequent in occurrence to warrant a call upon a medical practitioner and to alleviate temporarily physical or mental symptoms which may or may not be the danger signals of serious disorders.

The table illustrates the distribution of the annual national bill for medicines, classified according to the kinds of medicines purchased and the channels through which they reach the patients. It is apparent from the table that the pharmacy, or "drug store," dominates the sale and distribution of medicines in the United States: $625,000,000 is spent by the public for medicines purchased in pharmacies or drug stores, indicating that these agencies control more than 87 per cent of all sales of drugs and medicines. All the sales of other retail agencies—mail-order houses, general stores, medicine venders—represent medicines for self medication. These agencies account for $40,000,000, or 6 per cent of the total bill. Physicians and medical institutions (hospitals and dispensaries) make purchases of medicines equal in each case to $25,000,000, or approximately 3½ per cent of the total national bill for medicines. These latter purchases are classified as "physicians' prescriptions," because of the fact that they are administered or dispensed in accord with the instructions of medical practitioners. As a rule, such medicines are either given free to patients, or are charged for under such conditions that the sale price to the patients cannot be determined.

DISTRIBUTION OF THE ANNUAL NATIONAL BILL FOR MEDICINES IN THE UNITED STATES

Type of medicine.	Distributing agent.				
	Drug stores (pharmacies).	Other retail agencies.	Physicians.	Hospitals and dispensaries.	Total.
Physicians' prescriptions	$140,000,000	. . . . . .	$25,000,000	$25,000,000	$190,000,000
Home remedies	150,000,000	$15,000,000	. . . .	. .	165,000,000
Patent medicines	335,000,000	25,000,000		.	360,000,000
Total	$625,000,000	$40,000,000	$25,000,000	$25,000,000	$715,000,000

The total amount spent for drugs and medicines is of the same general magnitude as the total annual outlay for the services of physicians or for hospitalization, and it far exceeds the combined amount paid to nurses, dentists, and secondary and sectarian practitioners. Actually the expenditures for medicines represent, on the average, between $20 and $25 per family per year.

In this machine age the manufacturing function in the pharmaceutical field has been absorbed largely by the manufacturing pharmacist. The individual apothecary is still called upon to prepare medicines prescribed by physicians to meet particular conditions, but he no longer makes up in his laboratory the quinine pills, the elixirs, tinctures, extracts, and a multitude of other preparations that enter into physicians' prescriptions. Thus the function of the pharmacist has not changed, but his base of operations, as far as manufacturing goes, has been changed from the back room of the drug store to the laboratory of the manufacturing pharmacist. The drug store is still a place where extemporaneous prescriptions of physicians are compounded, but the ingredients from which the prescriptions are made usually come from a manufacturing laboratory, where analytical "control" and the assay of finished products play an important part in assuring the physician that the remedy he prescribes will reach the patient in its most potent and presentable form. In the manufacturing laboratory, the pharmacist is a manufacturer. In the retail drug store, he is a compounder and dispenser. These divided functions overlap at times, but they are becoming more and more distinct as time goes on. It is hardly conceivable that the need for extemporaneous prescriptions will ever be eliminated. It is certain, however, that less and less manufacturing will be done by the prescription pharmacist, and that supplying simple and mixed pharmaceuticals in ready dosage forms, such as tablets, capsules, ampuls, etc., will increase to the point where extemporaneous compounding will be materially reduced.

The professional pharmacist is, therefore, in much the same position as the general practitioner of medicine. Like the general practitioner of medicine, he finds himself in a position where he cannot possibly be an expert in all phases of his profession. He therefore specializes in one particular phase, to the virtual exclusion of all others. The specialties include compounding and dispensing, which is chosen by the greatest number, and may be compared to "general practice" in the medical field; manufacturing, which may again be subdivided into chemical, pharmaceutical and biological; wholesaling; drug collecting; "control" work; teaching; administration; and law enforcement.

The fact that specialization has entered the field of pharmacy does not decrease the responsibility of the general practitioner—the retail pharmacist—for acquiring and maintaining a general knowledge of the entire professional work with which he is identified.

In the succeeding chapters the student of pharmacy is made acquainted with the principles of pharmacy which underlie its practice. These principles are developed in the discussion of preparations and drugs listed in the U. S. Pharmacopœia and National Formulary and in the exposition of the art of compounding and dispensing prescriptions.

Pharmacy Defined.—The study of pharmacy includes the study of the theories and exercise of the operations necessary to the intelligent preparation and dispensing of substances used in the healing art. The two Greek words designating this idea were *pharmacon*, "a drug, a medicine, remedy, a potion, charm, spell," and *apotheke*, "a repository; a storehouse." The first of these roots has been anglicized into such words as *pharmacy*, the art of preparing, preserving, compounding, and dispensing medicines, and *pharmacist*, one skilled in pharmacy; while from the second we get *apothecary*, one who practices pharmacy. The word, *drug*, comes from the Anglo-Saxon "dryge" which means "dry;" hence a dry herb. Another word derived from the first-named root is pharmacopœia; *pharmacon*, "medicine," and *poiein*, "to make"; literally, "the making of medicines," but now used to designate a book of medical recipes prepared or approved by the government of the country where published. The history of pharmacopœias involves the history of pharmacy, for as pharmacopœias evolved from crude handbooks of medical lore to the present works of high scientific value, even so has the practice of pharmacy progressed from the jumbling of crude and often disgusting ingredients, of which the manipulator knew but little, to the modern blending of carefully refined constituents into standardized medicaments of which the operator knows not only the past history, but also the future action, both chemic and therapeutic.

PHARMACOPŒIAS AND OTHER BOOKS ON PHARMACY

The earliest prescription now extant is a stone tablet in the British Medical Museum, the approximate date of which is 3700 B. C. The earliest works answering to a pharmacopœia are Egyptian papyri, such as Papyrus No. 37 of the Berlin Museum, which is a fragment from 1700 B. C., and from its historic references seems to be a copy of a manuscript of 4000 B. C. In it five forms of medicine—ointments, liniments, poultices, clysters, and potions—are mentioned. The famous Ebers Papyrus, while of later date (1550 B. C.), is peculiarly valuable because of its completeness. In it mention is made of such drugs as calamus and myrrh, salt and sodium carbonate, while its list of preparations includes all given in Papyrus No. 37, among others, pills, mixtures, and decoctions.

Passing down to classic times, we find many medical works (written by individuals) which may be classed among the pharmacopœias, such as books of Hippocrates (460–377 B. C.), Dioscorides (either first or second century of the Christian era), and Galen (A. D. 131–201). These books were considered as standards by physicians for many centuries, scarcely being replaced until the appearance of the works of Paracelsus and of other medieval writers. Among the medieval works of medicine worthy of special note, mention should be made of the "Antidotarum" of Nicholas Preposit approved by a decree of Fredrick II in 1224; of the "Ricettario," published by the College of Medicine of Florence (1498), and the "Pharmacorum Omnium" of Valerius Cordus (1546). The latter work, published by the city of Nuremberg after the death of the writer, began a series of municipal pharmacopœias, such as those of London (1618), Paris (1639), Edinburgh (1699), which answered the requirements of the age of municipal isolation, but as means of transportation improved and people traveled freely to and fro, it was found that the difference in pharmacopœias was productive of confusion; that, for instance, a traveler from Nuremberg having his prescription compounded in Frankfort was in danger of an excessive dose of a potent preparation, there being no uniformity in the preparations of the different municipal pharmacopœias. Accordingly, a demand for national pharmacopœias grew, and the first to appear was the Codex Medicamentarius, published by the French government in 1818, the successor of the Paris Pharmacopœia, with its authority extended through all of France.

The next national pharmacopœia was that of the United States, published in 1821. The merging of the pharmacopœias of London, Edinburgh, and Dublin into the British Pharmacopœia did not occur until 1864, while in Germany the municipal pharmacopœias were replaced first by those of the States of Germany (Prussia, Hanover, Saxony, etc.), and these merged into the national authority in 1872.

At the present time there are some twenty national pharmacopœias in force, including those of every country of Europe (save some of the Balkan States and Turkey), the United States, Argentine, Chili, Venezuela and Mexico representing Latin America, and Japan representing Asia. Canada and other colonies of England use the British Pharmacopœia.

Even as the municipal pharmacopœias of preceding centuries caused confusion as the means of communication improved, today, when it is easier to travel from New York to Berlin than it was to go from Munich to Berlin a hundred years since, we are confronted by the confusion of the several national pharmacopœias. Thus every year thousands of Americans travel abroad, taking with them the prescriptions of their American physicians, and if the prescription calls for a tincture, it is quite likely that the tincture dispensed in good faith by the French pharmacist may be of entirely different strength from the American preparation, because made according to the French Codex. A most startling example of this kind was formerly illustrated by that potent preparation, tincture of aconite root. Thus in the nineties, the United States Pharmacopœia directed that 100 cc. represent the active strength of 35 Gm. of drug (35 per cent); the tincture of the German Pharmacopœia was but 10 per cent; the French Codex directed it to be 20 per cent; while the strength of the British was 12 per cent. It is self evident what dangerous results would have ensued if an American pharmacist had dispensed the tincture of the United States Pharmacopœia on a prescription written by a German physician; hence it is the duty of every pharmacist to acquaint himself with the strength of foreign preparations by reference to dispensatories.

This diversity of strength has called forth a demand for an *international pharmacopœia*, including at least preparations of all the potent drugs, so that one strength—say of tincture of aconite—be authorized by all the national pharmacopœias, and thus the same preparation be dispensed at all pharmacies in the world. This question was discussed at the first international pharmaceutic conference held in Brunswick in 1865, and has been brought up at every subsequent conference (Paris, 1867; Vienna, 1869; St. Petersburg, 1874; London, 1881; Brussels, 1885; Chicago, 1893; Brussels, 1897; Paris, 1900; Brussels, 1910; The Hague, 1913), but little progress in that direction has been accomplished. One of the first practical moves beyond the stereotyped resolutions and preliminary drafts was the action in 1893 of the American Pharmaceutical Association in donating $1000 to the international conference for defraying the expenses of compiling, publishing, and distributing such a work, and, lastly, in 1902 a conference of delegates appointed by the States of Europe and by the United States met in Brussels and decided upon a list of forty-three drugs and preparations which they recommended to the pharmacopœial commissions of all the countries of the world for adoption in the next edition of the pharmacopœia of each country. This list was enlarged to include seventy-seven drugs and preparations at the second Brussels Conference held in 1925.

Thus, among others, was the recommendation that tincture of aconite and tinctures of other potent remedies be placed at a uniform strength of

10 per cent in all the pharmacopœias of the world. Another recommendation was that syrup of ferrous iodide be made so as to contain 5 per cent of ferrous iodide.

Those official preparations conforming to the requirements of the Brussels Conference are designated in the present United States Pharmacopœia by a special synonym followed by the initials "P. I."—*protocol internationale.*

The committee preparing the tenth revision of the Pharmacopœia of the United States embodied in that standard many of the forty-three recommendations of the second Brussels Conference and the committee preparing the U.S.P. XI has retained most of them. The same step is being taken by other national pharmacopœial commissions thus tending to make preparations of potent remedies the same strength the world over.

Turning to our own standard, the *Pharmacopœia of the United States*, this important work was inaugurated by Dr. Lyman Spalding of New York, who in 1817 started the movement by suggesting that the country be divided into four districts, and all medical colleges and medical societies in each district be invited to send delegates to a district convention which should form an outline of a pharmacopœia. Each convention, in turn, should send delegates to a national convention which was, indeed, held at the capitol in Washington on January 1, 1820. At this convention two drafts of prospective pharmacopœias were submitted, and these were compared, consolidated, and revised in convention and ordered published, and in the following December there appeared the first Pharmacopœia of the United States. The convention of 1820 arranged that a revision should occur in 1830, by ordering the four districts to elect and send three delegates each to a convention to be held in Washington on January 1, 1830. The method of election of these delegates resulted in a misunderstanding and the holding of two conventions and publishing of two pharmacopœias; the officers of the convention of 1820 holding a poorly attended meeting at New York. The malcontents held a convention at Washington, at which the surgeon-general of the army and the senior surgeon of the navy and three members of Congress were present, thus giving indirect governmental authority to the pharmacopœia so issued. Another important step was the intrusting of the publication of the revised pharmacopœia to a committee of revision of seventeen members rather than preparing a hurried work on the floor of the convention. This pharmacopœia appeared in 1831.

The convention of 1840 was arranged by the Washington convention of 1830 along the lines followed to this day. Every incorporated medical society and medical college was invited to send three delegates to the convention, which met the first Monday in January.

Twenty delegates were present, and a committee of revision of seven members was elected. This committee was authorized to ask the coöperation of the pharmacy colleges in the work of revision, and, furthermore, the convention directed the presiding officer to invite the colleges of pharmacy to send delegates to the 1850 convention, which was called for the first Monday in May. The pharmacopœia was issued in 1842 and directed the process of percolation for the first time.

At the convention of 1850 pharmacists were present as delegates for the first time, and there were thirty delegates in all. A committee of four was elected to revise the pharmacopœia, and the fruit of their labor was published in 1851. The convention of 1860 was attended by thirty delegates, and a committee of revision of nine members published the pharmacopœia in 1863.

Sixty delegates were present at the convention of 1870; a revision committee of fifteen members was appointed and given general instruction as usual, and arrangements were made for the calling of the next convention.

At the convention of 1880, 109 delegates were present, representing thirty-five medical and eleven pharmaceutical bodies and the committee of revision chosen consisted of eleven physicians and fourteen pharmacists. To the convention of 1890, delegates from the various State pharmaceutical associations were invited, and accordingly fifty medical bodies and fifty-nine pharmaceutic organizations were represented; the committee on revision chosen consisting of ten physicians and sixteen pharmacists. Seated at the convention of 1900 were delegates from fifty-seven medical and fifty-nine pharmaceutic bodies and there was elected a revision committee consisting of six physicians and nineteen pharmacists.

At the convention of 1910, in addition to delegates from government bureaus, from the American Dental Association, the American Chemical Society and from the national food chemists' associations there were represented seventy-seven medical and seventy-four pharmaceutical bodies. The committee of revision was enlarged to fifty members and the work was subdivided among fifteen sub-committees. The chairmen of each of these fifteen sub-committees were constituted an executive committee of revision, to which the intimate details of revision was entrusted. This committee of revision consisted of twelve physicians and thirty-eight pharmacists.

At the convention of 1920, 286 delegates from forty-one medical bodies, eighty-one pharmaceutical bodies, five government bureaus and two other scientific organizations of national scope were present. The revision committee by mutual agreement organized with a membership of seventeen physicians and thirty-three pharmacists. The convention was presided over by Dr. Harvey W. Wiley, the champion of federal food and drug legislation. The important sub-committee on scope to which was delegated the responsibility of selecting the therapeutically active substances to be admitted consisted of sixteen physicians and five pharmacists. The twenty-one physician members of the revision committee were constituted a "Referee Committee on Scope" for deciding disputed questions involving the admission of substances of therapeutic value. Auxiliary members to sub-committees were added for the first time in this revision thus making available many experts to the committee who were not members of the revision committee. The Tenth Revision became official January 1, 1926 and was translated into Spanish for use in Cuba and Central and South American Republics. Four supplements or "Interim Revision Announcements" were issued prior to the advent of the U.S.P. XI. This is a departure which will probably be followed to a greater extent from now on because of the rapid development of new therapeutic agents requiring more prompt *official* standardization than is possible through decennial revisions.

The 1930 convention was attended by 413 delegates and was presided over by Dr. Reid Hunt. A revision committee of fifty-one was elected, including the President of the Convention ex-officio. The distribution of membership as between pharmacal and medical representatives was the same as for the previous convention. The revision committee has made the U.S.P. XI conform to many new developments in therapeutics which will be pointed out in the succeeding pages.

To the American pharmacist, the study of the history of his pharmacopœia should be a source of satisfaction and pride, as therein he will note the gradually increasing influence of the pharmacist in the framing of his national pharmacopœia. In 1820 the work was done by physicians only; in 1910 the pharmacists on the revision committee outnumbered the physicians two to one and while the 1930 revision committee can boast of but two retail pharmacists, the representatives of pharmaceutical associations and colleges again outnumber those of medical societies and colleges considerably. Moreover, each pharmacist should appreciate that he can have direct voice in saying who shall revise his pharmacopœia, as every reputable pharmacist is eligible to membership in his State pharmaceutical association, and at the meeting prior to the convention an election of delegates to the convention is held.

As mentioned in the definition on p. 26 a modern pharmacopœia differs from other books on medicine by being either published by the government or by receiving governmental approval. In England and in Germany, for example, the pharmacopœia is prepared by commissions appointed by the government. In this country the national government has nothing to do with the publication of the pharmacopœia, except sending delegates from the medical, pharmaceutical and other scientific branches of the federal service. Of late years the pharmacopœia has attained national importance, since not only is it used in government hospitals and dispensaries, but also is mentioned in the Federal Food and Drug Law of 1906 and the drug laws of the various States as the standard for identity, purity, and strength which all articles bearing an official title and intended for medicinal use must meet. The official assay processes thus become the standard methods by which the quality of drugs is measured by government officials.

In the United States, any drug or medicine recognized by the pharmacopœia or by the National Formulary is said to be *official,* which term has largely replaced the term *officinal,* which up to the present century was used to convey the same idea.

THE UNITED STATES PHARMACOPŒIA AS A BOOK

Before taking up the monographs of the pharmacopœia on individual drugs, it is well to devote a short space to the work as a whole, and this can best be done by copying in its entirety information found in our national standard relating to four typical officials.

In the comparative table on p. 31 (*a*) is the Latin name, (*b*) the English name, (*c*) the official abbreviation, (*d*) the synonym, (*e*) the chemical formula and molecular weight, if any, (*f*) the official definition, (*g*) the recipe and method of manufacture, (*h*) the official description and physical properties, (*i*) the tests for identity, (*j*) the tests for purity, (*k*) the assay process, if any, (*l*) the method of storage, (*m*) the alcohol content, if any, (*n*) the preparations which the drug enters and (*o*) the official dose. In case of preparations, the recipe for compounding is usually given, as (*g*), under Tinctura Lavandulæ Composita.

These several parts of the pharmacopœial monograph on a drug are not all included in every monograph because of the variation in source and type of drugs listed. They can best be discussed in regular order.

The **Latin name** is placed first in the United States Pharmacopœia for the several reasons that are given in discussing the use of Latin in prescriptions (p. 1039) and the name chosen is usually the simplest and clearest title found among the several Latin designations of the drug.

(*a*) **VERATRUM VIRIDE**

(*b*) **Veratrum Viride**

(*c*) **Verat. Vir.**

(*d*) **Green Hellebore, American Hellebore**

(*f*) Veratrum Viride consists of the dried rhizome and roots of *Veratrum viride* Aiton (Fam. *Liliaceæ*).

Veratrum Viride contains not more than 5 per cent of its stems or other foreign organic matter, and yields not more than 4 per cent of acid-insoluble ash, page 473 (U.S.P.).

(*h*) **Description and Physical Properties**—

Unground Veratrum Viride.—Rhizome more or less conical, from 2 to 7 cm. in length, from 1.5 to 3 cm. in diameter, externally light to dark brown or brownish-black; frequently bearing at the summit numerous, thin, closely-arranged leaf bases, otherwise rough and wrinkled and somewhat annulate from scars of bud scales; inodorous; taste bitter and acrid. Roots numerous, nearly cylindrical, from 3 to 8 cm. in length and from 1 to 4 mm. in diameter, usually transversely wrinkled, brittle, whitish, and more or less starchy.

Structure.—The rhizome shows an outer layer of brownish corklike cells; parenchyma containing raphides of calcium oxalate and starch; layer of endodermal cells broken in places by leaf-trace bundles; vascular bundles arranged in interrupted circles, single bundles scattered throughout the central parenchyma and also in the cortex.

The root shows epidermal cells with lignified thickened outer and radial walls; parenchyma similar to that of rhizome but interspersed with large irregular cavities in the outer regions of the cortex; endodermal cells with inner and radial walls thickened and slightly lignified, with U-shaped cavity about one-third the cell width.

Powdered Veratrum Viride.—Grayish-brown to dark brown, strongly sternutatory; starch grains numerous, from 0.003 to 0.020 mm. in diameter, spherical or ellipsoidal, single or 2- to 3-compound; raphides from 0.015 to 0.150 mm. in length; tracheæ scalariform or reticulate, often with lemon-yellow contents and associated with slightly lignified porous fibers; cork fragments few, reddish-brown or brownish-black.

(*n*) **Preparation.**—Tinctura Veratri Viridis.

(*o*) **Average Dose.**—Metric, 0.1 Gm.—Apothecaries, 1½ grains.

(*a*) **SULFUR SUBLIMATUM**

(*b*) **Sublimed Sulfur**

(*c*) **Sulfur Sublim.**

(*d*) **Flowers of Sulfur**

(*f*) Sublimed Sulfur, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of S.

(*h*) **Description and Physical Properties.**—A fine, yellow, crystalline powder having a faint odor and taste.

Sublimed Sulfur is practically insoluble in water, and nearly insoluble in alcohol. One Gm. of it dissolves slowly and usually incompletely in about 2 cc. of carbon disulfide. One Gm. of Sublimed Sulfur is soluble in about 150 cc. of ether, and in 100 cc. of olive oil.

(*i*) **Tests for Identity.**—Sublimed Sulfur burns in the air to sulfur dioxide, which can be recognized by its characteristic odor.

(*j*) **Tests for Purity.**—The residue upon ignition does not exceed 0.5 per cent.

(*k*) **Assay.**—Dry about 1 Gm. of Sublimed Sulfur to constant weight over sulfuric acid, weigh accurately, and transfer it to a flask containing 50 cc. of an alcoholic solution of potassium hydroxide (1 in 10). Boil the mixture until the liquid is transparent and the Sulfur is dissolved, then dilute it with distilled water to measure exactly 250 cc. Oxidize 25 cc. of this dilute solution by the addition of solution of hydrogen peroxide in excess (using about 50 cc.), heat on a water bath for thirty minutes, acidulate the liquid with hydrochloric acid, dilute it with 250 cc. of distilled water, heat to boiling, and add hot barium chloride T.S. in small portions to the resulting liquid until no further precipitation takes place. Heat this mixture on a water bath for thirty minutes, collect the resulting precipitate, wash, dry, ignite, and weigh it. Carry out a blank determination, using the same quantities of reagents but omitting the Sulfur, and before making the final calculation deduct the weight of barium sulfate thus obtained from that obtained in the assay. The weight of the barium sulfate thus obtained, multiplied by 0.1373, indicates its equivalent of sulfur. Each Gm. of Sublimed Sulfur, previously dried, is equivalent to not less than 7.281 Gm. of $BaSO_4$.

(*n*) **Preparation.**—Sulfur Lotum.

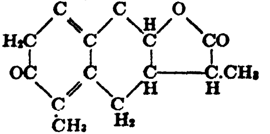
(*o*) **Average Dose.**—Metric, 4 Gm.—Apothecaries, 1 drachm.

(*a*) **SANTONINUM**

(*b*) **Santonin**

(*c*) **Santonin.**

(*e*) $C_{15}H_{18}O_3$



Mol. wt. 246.14

(*f*) The inner anhydride of santoninic acid.

(*h*) **Description and Physical Properties.**—Colorless crystals, usually tabular, or a white, crystalline powder. Santonin is odorless, and nearly tasteless at first, but afterward develops a bitter taste. It is stable in the air, but rapidly becomes yellow on exposure to light.

Santonin is almost insoluble in cold water, and only slightly soluble in boiling water. One Gm. of Santonin is soluble in 43 cc. of alcohol, and in 1.7 cc. of chloroform, at 25° C. One Gm. is soluble in 6.5 cc. of boiling alcohol.

(*i*) **Tests for Identity.**—Santonin melts between 169° and 171° C., page 455 (U.S.P.).

A solution of Santonin in alcohol (1 in 50) is neutral to litmus paper.

Solutions of Santonin are lævorotatory, page 459 (U.S.P.).

Heat about 0.2 Gm. of Santonin with 2 cc. of alcoholic potassium hydroxide T.S.: the mixture develops a red color.

Shake about 0.01 Gm. of Santonin with a cool mixture of 1 cc. each of sulfuric acid and distilled water, heat the solution to 100° C., and add a drop of dilute ferric chloride solution (1 volume of ferric chloride T.S. to 10 volumes of distilled water): the mixture is violet in color.

(*j*) **Tests for Purity.**—Ash: not more than 0.1 per cent, page 439 (U.S.P.).

The solution produced by dissolving 0.1 Gm. of Santonin in 5 cc. of sulfuric acid has no more color than matching fluid O, described under the test for *carbonizable substances*, page 441 (U.S.P.).

Boil 0.5 Gm. of Santonin with 20 cc. of distilled water and 2 cc. of diluted sulfuric acid, cool, and filter the mixture: the addition of mercuric potassium iodide T.S. or of iodine T.S. to 10 cc. of the filtrate, mixed with 10 cc. of distilled water, produces no cloudiness even after standing for three hours (*alkaloids*).

(*l*) **Storage.**—Preserve Santonin in well-closed containers and protected from light.

(*o*) **Average Dose.**—Metric, 0.06 Gm.—Apothecaries, 1 grain.

(*a*) **TINCTURA LAVANDULÆ COMPOSITA**

(*b*) **Compound Tincture of Lavender**

(*c*) **Tr. Lavand. Co.**

(*d*) **Compound Spirit of Lavender**

(*g*)

Oil of Lavender	**8 cc.**
Oil of Rosemary	**2 cc.**
Cinnamon, in moderately coarse powder .	**20 Gm.**
Clove, in moderately coarse powder	**5 Gm.**
Myristica, in moderately coarse powder .	**10 Gm.**
Red Saunders, in moderately coarse powder.	**10 Gm.**
To make	**1000 cc.**

Prepare a tincture by Process M, page 391 (U.S.P.), macerating the mixed powders in a mixture of 750 cc. of alcohol, in which the oils have been dissolved, and 250 cc. of distilled water. Complete the preparation with a menstruum of 3 volumes of alcohol and 1 volume of distilled water.

(*m*) Alcohol Content.—From 67 to 72 per cent, by volume, of C_2H_5OH.

(*o*) Average Dose.—Metric, 2 cc.—Apothecaries, 30 minims.

In this respect our pharmacopœia is a great improvement over those of most other countries, where lengthy Latin titles seem the rule. In the pharmacopœia of our country but one word is used for the Latin name whenever possible; thus, it calls aconite "*Aconitum*," and not "*Tubera Aconiti*," as does the German Pharmacopœia, there being but one part of the aconite plant recognized by the United States Pharmacopœia; hence there is no confusion in the single name. Of course, one word as the Latin name would sometimes lead to confusion; thus, two parts of the belladonna plant are official—the root and the leaf. The single word belladonna immediately gives rise to the question, "which part of belladonna?" hence, in such cases to the Latin word is added the name of the part, viz., *Belladonnæ Folium and Belladonnæ Radix*. Again, as another case, there are two mints official—the herbs, *Mentha Piperita* and *Mentha Viridis* respectively. To call either *Mentha* would be confusing, hence the Latin titles of the two are as just given. In choosing the Latin name of a vegetable drug the United States Pharmacopœia usually selects the generic name (p. 34) of the plant from which it is derived, one exception being *Cascara Sagrada*, the botanical name of which is *Rhamnus Purshiana*. Among the chemicals, the same simplicity obtains in the United States Pharmacopœia, although, as it is impossible to express the idea of acids and salts in less than two words, one-word Latin names are very infrequent. As also obtains in the case of vegetable drugs, there are some instances where extra words are needed to avoid confusion. Thus, there are two official forms of iron and ammonium citrate—garnet-red and green. They are listed as *Ferri et Ammonii Citrates* and *Ferri et Ammonii Citrates Virides*, respectively. Likewise, there are two official sodium phosphates in addition to the effervescent preparation of sodium phosphate—granular and dried; hence it is necessary to distinguish accurately between them. Therefore to the simple Latin phrase *Sodii Phosphas* is added the qualifying adjective "*Exsiccatus*" in the case of the dried salt whereas the granular product is known merely as *Sodii Phosphas*. In writing these Latin names the accepted rules of Latin grammar are followed, as will be shown later (Chapter LVIII). Here it suffices to say that all the Latin names of drugs are placed in the singular number—as galla, not gallæ, for nutgall, caryophyllus, not caryophylli, for clove—this, according to the United States Pharmacopœia of 1850, "following the example of the Roman medical writers."

English Name.—In choosing the official English name for the drug the revisers have not bound themselves to the most popular English designation for the same; in fact, as a rule, the popular names have been relegated to the class of synonyms, and in many cases as the English name has been chosen a term by which they are rarely known to the public; the official Latin and English names being very frequently the same. Thus, *Serpentaria* is given as both the Latin and English name of what is commonly known as *Virginia snakeroot* or *Texas snakeroot*. In choosing the English name, however, the same care and judgment were used as in the selection of the Latin name, and where the common English name is shorter than the Latin term and is sufficiently distinctive to preclude danger of confusion with other drug names, it is then chosen; thus, "clove" is used instead of the Latin *Caryophyllus*; "ginger," instead of *Zingiber*; *Red Saunders* instead of *Santalum Rubrum*.

In choosing the English name of chemicals, the nomenclature of the Geneva International Conference on chemical names has been followed in many cases, the aim being to be thoroughly modern without being ultra-advanced. Of this nomenclature of salts, particular reference will be made in Chapter XXII, so here need only be mentioned the advisability of the student accustoming himself to the modern naming at the outset of his studies. Thus, learn to use the modern term "potassium chlorate" instead of the antiquated title "chlorate of potassium," or, worse yet, "chlorate of potash."

Official Abbreviation.—This innovation, the insertion in the pharmacopœial text of abbreviations of the Latin names of the medicines, is an idea that has not, as yet, justified its existence. It is very difficult to accustom oneself to arbitrary abbreviations such as are listed under the official titles.

Synonym.—Under this head the pharmacopœia places those drug names too popular to be ignored, and which, for various reasons, could, not wisely be accorded official preference.

The term "Virginia snakeroot" is almost universally employed instead of the official English name, "Serpentaria," but the pharmacopœia exercises selective preference for the latter word because the word snakeroot is applied to several distinct drugs, among them being: serpentaria; cimicifuga, or black snakeroot; caulophyllum, or Samson snakeroot; asarum, or Canada snakeroot; sanicle, or black snakeroot; eryngo, or button snakeroot; and senega, or seneka snakeroot. It is clear, therefore, that the designation snakeroot immediately raises the query, "which snakeroot?" hence the pharmacopœial aim to eventually do away with these confusing synonyms. Again, the use of the common synonyms is apt to bring misleading results by similarities in same. Thus, in one case, instead of calamus, recommended for the gums of a teething infant, calomel was purchased and applied. So the example set by the United States Pharmacopœia should be followed as far as possible by the retail pharmacist, who should endeavor gradually to educate his clientele to the official English name instead of the misleading and confusing synonym.

Chemical Formula.—A majority of the official chemicals are not derived from plant sources, hence in defining them a botanical name has no part, and a symbolic chemical formula is used instead.

A full explanation of a chemical formula will be given later, so sufficient for this place is the bare mention that it is an abbreviated method of expressing the composition of the chemical.

Thus the formula $NaCl$ means a compound consisting of one atom of the element sodium and one atom of chlorine to each molecule. K_2SO_4 means a compound containing two atoms of potassium, one atom of sulfur, and four atoms of oxygen to the molecule. Hence it can be seen that the chemical formula answers in place of a definition of many words. Moreover, by means of the symbolic formula we learn the exact composition of the official chemical. Thus, while absolute sodium sulfate is really Na_2SO_4, that is, it consists of two atoms of sodium, one atom of sulfur, and four atoms of oxygen to the molecule, the pharmacopœia gives as its symbolic formula, $Na_2SO_4.10H_2O$, showing that the official product is sodium sulfate combined with ten molecules of water of crystallization (Chapter XXVI).

The official definitions of chemicals in the present pharmacopœia are longer than those of former pharmacopœias, because of introduction of the so-called "*Purity Rubric.*" This includes a specific mention of the amount of absolute chemical contained in a commercial sample. Thus, sublimed sulfur (p. 31) "must contain not less than 99.5 per cent of S."

This purity rubric was introduced to define accurately the chemical for purpose of its identification under the Food and Drug Laws, both State and National. To say that sublimed sulfur is S would imply a 100 per cent product, which is practically impossible to obtain. Since the rubric directs "not less than 99.5 per cent," ½ of 1 per cent of accidental impurity, say, moisture, is permissible.

In the case of organic compounds the pharmacopœia now gives the structural formula as well as the condensed formula of each compound listed when the pure compound is official and the structural formula has been definitely determined. The molecular weight is also included.

Official Definition.—This tells what the drug is, and the United States Pharmacopœia does this in as few words as possible, as reference to the four typical cases given on page 31 will clearly show. Accordingly, as the drug is of vegetable or of mineral origin, the definition differs; in the first case, the botanical name of the plant yielding the drug plays a leading rôle in definition, whereas with chemical drugs the symbolic chemical formula is sometimes the entire definition. Hence it is profitable to discuss these two entirely different means of description separately.

Botanical Name.—Thanks to the science of botany, all the 175,000 plants known to the civilized world have been carefully studied, accurately classified, and to each has been given a distinctive scientific botanical name. This botanical name is of Latin form, and follows the rules of Latin grammar. It often seems unnecessarily long and difficult, but, as will be later shown, from time to time, it is usually aptly chosen, as by it we frequently can understand some of the characteristics of the plant. The botanical name of the plant generally consists of two words—the generic name, that common to the genus or plant group, and the specific name, peculiar to the one kind of plant under consideration, an adjective usually distinguishing it from closely similar plants.

Even to the English name of a plant we frequently have to add a qualifying adjective; thus we know two kinds of oranges, and to distinguish them we call one bitter orange, the other, sweet orange; so do they in Latin, the bitter orange being *Citrus Aurantium*, the sweet orange being *Citrus Aurantium* var. *sinensis*. The lemon is very similar to the orange, hence is given the same generic name, its complete name being *Citrus medica* var. *Limon*. In fact, botanical names are very much like our personal names. We are Smiths and Jones and Browns because we belong to these families, and in order that one Smith may be distinguished from another, we call each by what is known as a given (or Christian) name—Tom, Dick, or Harry. The difference between the personal names of men and the botanical names of plants is that in plants the specific name, the plant's "Christian name," is put last instead of first, as if we would call ourselves Smith John, instead of John Smith.

Do not misconstrue the above comparison of the family name Smith to the botanical name Citrus into the idea that the word Citrus is the family name of the plant. It is the name of the *genus*; a plant *family* being much broader, and including many genera.

As to the writing of the botanical name, the generic name always begins with a capital letter, while the specific name is written with a small initial letter, except in three cases: (1) when the specific name has been at one time the generic name; (2) when derived from the name of a person; (3) when an indeclinable noun. As seen above, in some cases, the specific name consists of two words; one designating the particular variety, when there are two or more varieties of the same species.

Following the botanical name in the United States Pharmacopœia and other standard works comes a proper name—as, "*Cinchona succirubra*, Pavon" or "*Pterocarpus santalinus*, Linné filius." This is the name of the botanist by whom the botanical name was bestowed upon the plants. A glance through the pharmacopœia will show that a large number of plants were examined and named by Carl von Linné (1707–1778), who was a Swedish physician and teacher of pharmacy. The botanical term *family*, mentioned above, and used in the present pharmacopœia, was scarcely happily chosen, and in common conversation it is better to use the word "tribe" instead. Scientists substitute for the word the term "natural order." For complete explanation of this plant grouping recourse should be had to a standard botany, so suffice it here to state that similar plants are grouped together into a *genus* (plural, *genera*); thus all the roses are grouped into the genus *Rosa;* the oranges and the lemons into the genus *Citrus;* the mints into the genus *Mentha.* Now, roses have some characteristics like those of the blackberries (or the genus *Rubus*), and, like the apples and pears (or the genus *Pyrus*). In such cases these similar genera are grouped together for classification into a natural order; in that under consideration the name chosen for the natural order is *Rosaceæ.* Similarly, the daisies (genus *Bellis*), the sunflowers (genus *Helianthus*), the dandelions (genus *Taraxacum*), and many similar genera are grouped into one natural order called the *Compositæ.* It will be noticed in the United States Pharmacopœia the botanical name is always followed by the name of the natural order (or family).

Method of Preparation.—Of the 568 pharmaceuticals recognized by the United States Pharmacopœia, in the case of about 27 per cent the method of preparation is given, the policy being to give a recipe whenever it is practical for the pharmacist to compound the remedy. For heavy chemicals, which can be made much more cheaply by the large manufacturer than by the retailer, no recipe is given. Recently it has also become the policy not to include a method of manufacture if more than one satisfactory method is available, because the federal government has ruled under the Food and Drug Act that where a pharmacopœial method is prescribed it must be used regardless of the fact that a finished product made by some other method can be produced to give the same tests for identity, purity, and strength.

The recipes of the United States Pharmacopœia are the result of careful study, and are as near perfect as human ingenuity can suggest. Occasionally an unpractical recipe slips in, but in most cases where a recipe yields an unsatisfactory product the fault lies with the manipulator, rather than with the framer of the recipe. In all recipes of the eleventh edition of the United States Pharmacopœia the metric system of weight is directed to be used, the transition from the old system occurring in the revision of 1880 and 1890, as can be noted by comparing the change in weights and measures in the pharmacopœias of 1870, 1880, and 1890:

1870. Troy ounce and fluidounce.

1880. Parts by weight (both solids and liquid weighed). This was done because of the strong desire to change from the old system—troy ounces and fluidounces—to the metric system.

However, the opposition to the innovation proved too strong, and, as a compromise, parts by weight were chosen. According to this, a preparation could be made either in avoirdupois ounces, troy ounces, avoirdupois pounds, troy pounds, grams, or kilograms. Thus, in the formula of Ammonia Liniment (1880) which read—

Water of ammonia	30 parts
Cotton-seed oil	70 parts

if we used ammonia water, 30 tr. oz., 30 av. oz. or 30 Gm., we would add respectively of oil, 70 tr. oz., 70 av. oz., or 70 Gm., giving everybody a chance to use his pet system of weights.

It proved, however, a bunglesome piece of work, for it was an awkward matter to weigh, for instance, 100 Gm. of a percolating tincture, but it accomplished its work. It established the idea of decimal ratio, and 1890 found the convention ready to adopt the metric system.

Since 1890. The metric system—grams and cubic centimeters.

Official Description and Physical Properties.—This division of the pharmacopœial treatment of official drugs scarcely needs extended comment, so clear and concise are the descriptions. They are inserted to enable the pharmacist to find out whether the drugs and chemicals he purchases are really of quality worthy of administering as medicine. With vegetable drugs, the description deals with the external and microscopic appearance of the whole and of the powdered drug.

Tests for Identity.—In the case of chemicals qualitative tests for both + and − ions are given as well as special identification tests and other tests such as melting point, boiling point, acidity or alkalinity.

Tests for Purity.—These include ash determinations, tests for limits of common impurities and absence of contaminants.

Assay Process.—In cases of some of the more potent drugs, a method of determining the quantity of the active ingredients is given, this method being called the *assay of the drug*. The assay process may involve gravimetric, volumetric, biological, colorimetric or other acceptable methods.

The neglect of the average pharmacist to compare his stock of medicines with the standards established by this pharmacopœial description is not only unwise, but also unsafe, for, aside from the ethical point that the pharmacist should never dispense a drug unless he personally knows that it is up to all pharmacopœial requirements, there is the selfish ground that in most of the States laws relating to the purity of drugs are in force and nothing is more fatal to the reputation of a druggist than prosecution for selling inferior drugs.

Method of Storage.—As many official substances are liable to deteriorate when carelessly stored, the Pharmacopœia in many cases gives explicit directions as to proper storing.

Alcohol Content.—In the case of those liquid preparations containing an appreciable amount of alcohol, the approximate alcohol content of finished preparation is stated in the monograph.

Official Preparations.—In the present pharmacopœia, the description or method of preparing an official product is followed by a list of those preparations of which it is an ingredient, a matter of much convenience to the student.

Average Dose.—As explained in the preface to the pharmacopœia, the dose given in most of the monographs on official products is intended purely as a guide to the practitioner and the dispenser. Efforts were made at the convention of 1910 to provide a table of maximum doses, beyond which the physician should not transgress, unless he emphasized his desire for heroic doses by writing out the amount in full or by other plain proof of his intention; but the proposition was voted down. The average dose stated is the quantity which may be expected ordinarily to produce the therapeutic effect for which the preparation is most commonly employed. Unless otherwise stated the dose is for adult human beings.

THE NATIONAL FORMULARY

This work prepared by a committee appointed by the American Pharmaceutical Association is now a legal standard since the National Food and Drug Law as well as most State laws, direct that the standards set for drugs and preparations found therein shall be employed in enforcing the several statutes. The sixth edition which appeared in 1936, contains not only a number of reliable recipes for well-known pharmaceuticals but also provides standards for all drugs used in making the preparations, when such ingredients are not recognized by the United States Pharmacopœia. In general the style and method of presentation of information follow those of the U. S. Pharmacopœia. The term "official" as applied to drugs and medicines includes those listed in the National Formulary. In the N.F. VI there are 689 monographs of drugs. Of these 390 are galenical preparations.

DISPENSATORIES

A pharmacopœia, being intended as a concise standard work of reference, by no means embraces all the material used in the healing art. Thus the eleventh revision, United States Pharmacopœia (abbreviated U.S.P. XI), recognizes drugs and chemicals, and these include scarcely a tenth of the remedies that have been suggested even in our country, exclusive, of course, of the nostrums. The officials represent those remedies which, in the judgment of the revision committee, are indispensable in the practice of medicine: those remedies singled out from the vast number as being really valuable. Even of official products the barest details are given by the various pharmacopœias in the effort to prevent these works from becoming too voluminous. Accordingly, in the various civilized countries there early sprang up the need of commentaries on the pharmacopœias: large works which not only fully described the official remedies, but also made mention of a large number of the unofficial drugs and chemicals used in medicine.

In this country such commentaries are called *dispensatories*, and we have been provided with three valuable works of this character: the United States Dispensatory, first published in 1833, the National Dispensatory, first published in 1879, and King's American Dispensatory, first published in 1854. Of these the first-named is the only one now kept up-to-date by regular revision.

BIBLIOGRAPHICAL HELPS

Among appliances needed by the pharmacist, none are more necessary than a well-selected library of books and journals, for it is from these that he learns the basic principles of his calling. In the preface will be found a list of such books and journals consulted by the author, with journal abbreviations used in the bibliography found at the end of each chapter.

As to books, these can be divided into three groups: (*a*) standard official works like the several pharmacopœias and the National Formulary; (*b*) "source books" distinguished by reason of their wealth of bibliographic references; and (*c*) books that are of service to the everyday druggist because of the practical information they offer on special lines. A suggestive list of this class is found in the *Druggists Circular* for April, 1914. As to "source books," most of those given in the bibliography found at the end of each chapter of this work are of that nature. In such, the seeker after the original articles can find the references to the papers he wishes to consult. Similar service is rendered by the Proceedings of the American Pharmaceutical Association volumes 1 to 60 (1851 to 1911) and in their successors the "Year Books" of the association and now in the monthly abstracts published in the *Journal of the American Pharmaceutical Association* which are to replace the Year Books. In current chemical literature, *Chemical Abstracts* published by the American Chemical Society is likewise of tremendous value, since therein are found abstracts of practically every article published in every chemical journal in the world.

BIBLIOGRAPHY

Commerce and Contemporary Pharmacy.—Rorem and Fischelis, The Costs of Medicines; U. S. Department of Commerce, National Drug Store Survey; Gathercoal, Prescription Ingredient Survey; F. A. Delgado, The Professional Pharmacy; Olsen, The Merchandising of Drug Products.

Etymology.—(Apotheke) Patton, A.Ph.A., 22, 1874, 343. (Pharmacopolæ) Rich, Dictionary of Greek and Roman Antiquities. Suppan, Jl. A.Ph.A., 20, 1931, 482. (Drug) Anon., Pract. Dr., 29, 1911, 32. Anon., D.-A. Ap. Zt., 41, 1920, 86. (Apothecary) Berendes, Nat. Dr., 40, 1910, 174. (Pharmacist) Bulwer-Lytton through Spatula, 16, 1910, 611.

History.—(General) Wootton's Chronicles of Pharmacy, 1910; Schelenz, Geschichte der Pharmazie; La Wall, Four Thousand Years of Pharmacy; Walsh, Am. Dr., 58, 1911, 37. Zornig, D.-A. Ap. Zt. 41, 1920, 1, 15, 29, 57, 71, 85, 99 and 113; Häussler, Schw. Ap. Zt. 57, 1919, 696; X-rayser II, Ch. and Dr. 88, 1916, 1199; Raubenheimer, Jl. A.Ph.A., 18, 1929, 268. (Egyptian) Mayo, Dr. Circ. 33, 1889, 76; Lippmann, Am. Dr., 57, 1910, 210. (Assyrian) Jastrow, Dr. Circ. 58, 1914, 415; Anon., Apoth., 41, Mch., 1929, 20. (English) X-rayser II, Ch. and Dr. 89, 1917, 217; Singer, Ch. and Dr., 111, 1929, 741. (French) Reutter, Schw. Ap. Zt., 53, 1915, 276 and 288; (Italian) Castiglioni, Ch. & Dr., 111, 1929, 748.

Pharmacopœias.—(General) Rice, Am. Dr., 16, 1887, 21, and Pharm. Era, 13, 1895, 36, 68 and 100; Tschirch, Schw. Ap. Zt. 53, 1915, 354, 367, 381 and 400. (U.S.) Wilbert, Motter and Du Mez, "Digest of Comments," Hygienic Laboratory Bulletins, Nos. 23, 49, 58, 63, 75, 79, 84, 87, 93, 98, 105, 119, 125, 127, 129 and 131; Scoville, Jl. A.Ph.A., 9, 1920, 280; (Dr. Lyman Spalding) Hurd, A. J. P., 91, 1919, 371. (Latin America) Wilbert, A.Ph.A., 58, 1910, 1218. (British) Anon., Dr. Circ. 58, 1914, 520. (Belgium) Motter, A.Ph.A., 58, 1910, 1146. (French) Dunning, A.Ph.A., 58, 1910, 1151. (German) Goetting, A.Ph.A., 58, 1910, 1151. (Hungarian) Dohme and Engelhardt, A.Ph.A., 58, 1910, 1107. (Japanese) Takamine, A.Ph.A., 58, 1910, 1195. (Netherlands) Kraemer, A.Ph.A., 58, 1910, 1202. (Spanish) Craig, A.Ph.A., 58, 1910, 1211. (Norwegian) Anon., Jl. A.Ph.A., 9, 1920, 926. (Swiss) Siegfried, Ph. Acta Helv., 5, 1930, 255. Abstract of Proceedings, U.S. Pharmacopœial Convention, 1910, 1920, 1930.

Botanical Nomenclature.—Drake, Schw. Ap. Zt., 53, 1920, 533; Gagnepain, Jl. de ph. et ch., 20, 1919, 202.

Geneva Conference.—Anon., Pharm. Era, 8, 1892, 43.

CHAPTER II

METROLOGY

METROLOGY is the science of weights and measures.

The definition of *weight* as commonly used, to express the quantity of a given substance, is erroneous, the correct word for the absolute quantity of matter in a given substance being *mass.*

Thus the mass of a substance is unchangeable under all circumstances, while the weight varies under certain influences, since weight is the measure of the gravitating force of the earth, and the gravitating force of the earth varies at different points on the earth's surface and interior.

Details as to gravity can be found in any text on elementary physics, so suffice it to say that all substances attract other substances in direct proportion to their mass, and since in the case of all bodies on the surface of the earth the mass of the earth is infinitely greater, the preeminent attraction is that of the earth.

That the earth attracts bodies to it is shown by every falling object, the tendency of the falling object being to attain as near the center of the earth as possible. An ocular demonstration of the quantity of gravitating force is offered by the Jolly spiral balance (Fig. 1), which consists of an exceedingly sensitive steel spring, which is elongated on placing at the end thereof a weight which is attracted downward by the earth's force. A rough application of this spiral balance is seen in the ordinary spiral butcher's scale or ice scale. Such a balance measures directly the force of gravitation, and hence the weight of the substance, since weight is the measure of the gravitating force of the earth.

The same spiral balance can be used for measuring the comparative weights of various substances at the same place on the earth's surface, but since the measure of gravitation varies at various points on the surface of the earth, such balances are intended for use only at the place for which they are standardized. Thus, a body which is attracted toward the earth with a force of 192 pounds at the poles, is attracted with a force of about 191 pounds at the equator. Hence, as stated above, the weight of a substance is not an absolute criterion of its quantity, and we should learn to speak of mass rather than of weight.

In measuring the quantity of substance, three systems of units may be employed—those of length, capacity, and weight—and while these systems seem to have been introduced in the order named, yet their origin is so ancient as to be lost in the mists of prehistoric days, the Jews claiming that both weights and measures were introduced by Cain.

As to measures, the most ancient is the Egyptian cubit—the length of the forearm (2300 B. C.).

The *foot* is of Grecian origin, legend saying that Hercules' foot served as model. *Inch* is of Roman origin, being an "*uncia*," or twelfth of a foot, and to the same people we are indebted for the *pace* and the *mile* (*millia passum*). The *yard* is more modern, being the Anglo-Saxon measurement of the girth.

Of weights, the oldest specimens now extant are those excavated from the ruins of Babylon and Nineveh; one of these, a stone duck, from 2007 B. C., is inscribed as representing ten "*manah*." This manah was evidently the standard for all neighboring countries, mention of it being made in the Bible. This manah was divided into 60 shekels, and weighed, in some cases, about one avoirdupois pound (489 to 502 Gm.), while others weigh exactly twice as much.

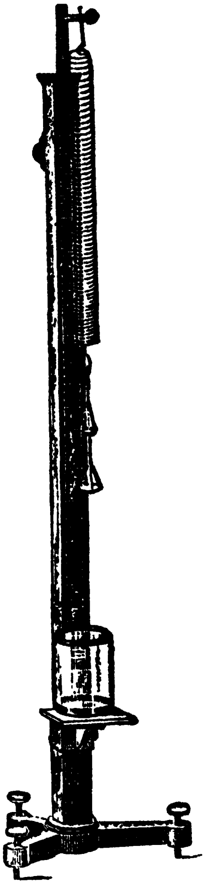


Fig 1 —Jolly's spiral balance.

This Babylonian manah was adopted by the Grecians, undergoing variations in weight during the lapse of years. Thus we find the city of Athens had a manah (or "mna," as they called it) weighing 15⅓ avoirdupois ounces (436 Gm.), and the same people had a silver coin weighing 1/100 of the manah, which they called "drachma."

The weight standards of ancient Italy seemed also based on the Babylonian manah, the first coins from Rome being masses of bronze weighing about one-third the heavy manah, and called the "*as libralis*," or "*pondo libralis*." This Roman pound was divided into halves, thirds, quarters, and twelfths, and the latter was called "uncia"—hence our word "ounce." Of the same monentary value of the bronze coin "as libralis" was a small silver coin weighing about twenty of our grains (1.137 Gm.), and this was called a "*scripulum*," and as time went on these coin weights became the standard weights of the nation, and so it was that at the time of Nero the Roman weights were a *libra*, or pound of 327 Gm.; 1/12 libra, or *uncia*; 1/8 uncia, or *drachma*; and 1/3 drachma, or *scripula*, practically our present apothecary system.

Concerning weights smaller than the scripula there is much confusion, different authorities mentioning the *obulus*, or 1/2 scruple; the *siliqua*, or 1/3 obulus, and the *chalkus*, or 1/13 obulus, or 1/5760 pound. This is of no special interest to us, and is mentioned merely to note the absence of the grain weight, although the siliqua (like our grain) was the weight of a seed—that of the plant *Ceratonia siliqua*, or St. John's bread.

The Roman weights were borrowed by all the countries of Central Europe, and likewise we find the coins of the middle ages were copies of those of Constantine the Great, whose Eastern Empire was a direct offshoot of the Roman. Thus the earliest Anglo-Saxon penny was an exact copy of Constantine's "tremisse," and weighs 1/3 scripula, or 24 grains, and the same is true of the penny of Alfred the Great. Evidently, this coin began to vary in weight, and to standardize same by some familiar unit was the aim of Henry III, whose statute of 1266 says the penny "shall weigh 32 wheat corns in the midst of the ear, and 20 pence do make an ounce, and 12 ounces one pound, and 8 pounds do make a gallon of wine, and 8 gallons of wine do make a London bushel." This famous statute is our formal introduction to our present system of weights and measures, giving us the first authentic reference to the pennyweight. The pound here mentioned is the ancient Tower pound, used from Anglo-Saxon times, and weighing but 5400 of our present grains.

The ordinance of Edward I (1304) reiterates the statute just given, directing a penny of 32 grains of wheat, the ounce of 20 pence, the pound of 12 ounces, the gallon of 8 pounds of wine, and the bushel of 8 gallons. It also contains the innovation that a pound of money and of medicine consist of only 20 shillings; a pound of all other things consists of 25 shillings. It furthermore adds that a pound of money contains 12 ounces, while a pound of all other things contains 16 ounces; that is, that articles of a common character should be dispensed with more lavish hand than those which were more expensive. Following this idea, this new system of weights for the coarser commodities was called "avoirdupois," from the French words "*avoir*" and "*pois*," which mean "to have weight." Hence the origin of two different pounds and two different ounces, thus entailing upon English-speaking people even to this day material inconvenience and discomfort.

But whence the change from the penny of 32 wheat grains to the penny of 24 of our present grains? No statute authorizing a penny of 24 wheat grains can be found, unless we accept the testimony of a single and somewhat questionable authority, that a statute of Edward I of the year 1280 directed a penny of 24 grains. The same authority believed that our present grain is the weight of a barley corn, rather than a wheat grain, and this may be the truth, since the grain of wheat of modern times has been found to weigh only three quarters of our modern grain, and likewise only three quarters the weight of a barley corn.

Be this as it may, it seems possible that our modern grain is a foreign weight replacing the wheat grain, just as our two pounds (troy and avoirdupois) are foreign units which gradually forced the ancient English standard, the Tower pound, from the field.

The first official record we have of the introduction of foreign systems is in a statute of 1314, where the phrase "pur la libre de *troy* orre" is used, this ordinance directing the price of metals by the troy pound; while a statute of 1335 authorized merchants to buy and sell "corn, wine, *avoirdupois*, flesh, fish," etc.; the word in this case has its original meaning of "weight articles," and it was not until a statute of 1529 that mention of "the weight called haverdupois" is made.

Of these two systems, the troy is supposed to have been the standard of the French city of Troyes, which was quite a commercial center in medieval days, while our present avoirdupois pound is said to have been the standard of Bayonne, another city of France.

The United States standard yard and troy pound date from 1760, they having been conferred upon the colonies by the mother country, and are copies of the ancient weights given above, and no change has been made by this government since its organization.

The exact number of grains in a gallon of distilled water has been the source of much controversy and varying values are given. One source of variation is the matter of temperature and of barometric pressure at which the estimation is made. Thus in U.S.P. IX, it was stated that the value taken at 25° C. and at 760 millimeters pressure is 58,185 grains, while at 4° C. and *in vacuo*, it is 58,416.6 grains; while in U.S.P. X and XI a gallon of water at 25° C. (no mention of barometric pressure being given) is said to weigh 58,184 grains. Of course, the weight of the pint and of fluidounce varies according to which figure is taken for the gallon.

In 1816 and in 1836 the British government modified its system of weights and measures, adopting the so-called Imperial system, in which an effort was made to place the accepted system of weights and measures on a scientific basis by comparing same with physical units which can be easily verified. Thus, the yard of 36 inches is based on the length of a pendulum beating seconds in a vacuum in London at 62° F. The length of this pendulum is 39.1393 of the accepted historic standard inches, and 12 of these inches are called a foot, and three feet, a yard. In other words, the Imperial inch and yard are the same lengths as the old units, but their determination has been placed on a careful physical measurement. In like manner the Imperial troy pound remains at the old standard, 5760 grains. The grains, however, were carefully determined by the weight of a cubic inch of distilled water, the weight of which at 62° F., and at 30 inches barometric pressure was found to be 252.458 grains. The Imperial gallon differs from the United States gallon, being the volume of 10 avoirdupois pounds of distilled water under standard conditions of temperature and barometric pressure. In other words, it is the weight of 70,000 grains of distilled water, and has the capacity of 277 cubic inches.

The volumetric subdivision of the Imperial gallon is also different from the United States gallon, it being divided, as ours, into 8 pints, but the pints are divided into 20 fluidounces instead of 16.

In our present United States system of weights and measures the troy, apothecaries', and avoirdupois ounce weights, and the yard and inch, are the same as the English, but the gallon, as the old English gallon of 1760, has a weight of 58,252.8 grains, and a capacity of 231 cubic inches.

The tables of weights and measures used in the United States are:

Apothecaries' Weight		Abbreviated
20 grains	= 1 scruple	℈
3 scruples	= 1 drachm	ʒ
8 drachms	= 1 ounce	℥
12 ounces	= 1 pound	lb.

Troy Weight		Abbreviated
24 grains	= 1 pennyweight	dwt.
20 pennyweight	= 1 ounce	oz.
12 ounces	= 1 pound	lb.

Avoirdupois Weight		Abbreviated
437½ grains	= 1 ounce	av. oz.
16 ounces	= 1 pound	av. lb.

U. S. Fluid Measure		Abbreviated
60 minims	= 1 fluidrachm	fʒ
8 fluidrachms	= 1 fluidounce	f℥
16 fluidounces	= 1 pint	O
2 pints	= 1 quart	qt.
4 quarts	= 1 gallon	Cong.

The résumé of the old system of weights and measures shows what confusion prevails. We see there are three distinct *ounces: avoirdupois*, 437½ grains; *apothecary* or *troy*, 480 grains; *U. S. fluid*, 454.6 grains of distilled water. Likewise there are two pounds: *troy*, 5760 grains; *avoirdupois*, 7000 grains. To this we now must add another confusion: two drachms, the apothecary drachm of 60 grains and, according to a Washington ruling, an avoirdupois drachm of 1/16 of an avoirdupois ounce or 27.34 grains.

Another pharmaceutic detail worthy of notice is the fact that pharmacists purchase their goods by the avoirdupois and dispense them chiefly by troy system. It is, therefore, well to remember that an eighth ounce of morphine sulfate is not an eighth of a troy ounce, or 60 grains, but an eighth of an avoirdupois ounce, or 54.69 grains.

As the English use the Imperial fluid measures: a fluidounce of 437.5 grains of distilled water and a gallon of 277 cubic inches or 70,000 grains of distilled water; both standards being different from the U. S. standards, American pharmacists should never use English glass graduates except in compounding British prescriptions.

COMMON MEASURES

The following common measures, largely used in the household, are worthy of mention:

A teaspoonful is supposed to be 1 fluidrachm.
A dessertspoonful is supposed to be 2 fluidrachms.
A tablespoonful is supposed to be 4 fluidrachms.
A wineglassful is supposed to be 2 fluidounces.
A teacupful is supposed to be 4 fluidounces.
A tumblerful is supposed to be 8 fluidounces.

The words "supposed to be" are well chosen, since most of the spoons and other measures vary greatly as to size.

Remember that a drop is not a minim, and a minim does not necessarily weigh a grain.

Drops vary according to the character of the liquid which is being dropped, and also according to the surface from which the liquid is dropped. As to the first, the variation in size of drops is from 44 drops of syrup of acacia, 120 drops of laudanum, and 250 drops of chloroform to the fluidrachm. The size of the drop of the same liquid will vary accordingly as the surface from which the liquid is dropped is sharp or flat, or whether the orifice from which it is dropped is large or small. Thus, water dropped from the bottom of a gallon evaporating dish measures 18 drops to the fluidrachm, whereas the same water at the same temperature dropped from a glass rod of 1/40-inch bore gave 600 drops to the fluidrachm.

Tate has calculated the size of the drop under varying physical conditions and has reduced his findings to a mathematical formula.

Official Medicine Dropper.—The U.S.P. XI prescribes an official medicine dropper and states that such dropper shall have its delivery end 3 millimeters in external diameter, and be adjusted to deliver 20 drops of distilled water, weighing 1 gram at a temperature of 15° C. A tolerance of 10 per cent below or 10 per cent above the delivery specifications is permitted.

THE METRIC SYSTEM

The confusion resulting from the use of units of the same name and of different values cited on preceding pages led to an effort to secure an international system of weights and measures. This movement was instituted by Prince de Tallyrand, who persuaded the French assembly to pass a bill providing for the collating of the various systems of weights and measures then in use in France, requesting the cooperation of the British government, and assigning the formation of the new system, based on a universal standard, to the French Academy of Sciences. The French Academy took up the work, and the report of same was made into a law August 1, 1793. The next year the French government sent the United States government a copy of the new weights and measures, with the request that they be adopted by the infant republic; this request was communicated to Congress by President Washington in his message, January 8, 1795. In 1821 national attention was brought to the metric system by John Quincy Adams, in a comprehensive report to Congress, but nothing was done on the subject by that body until 1866, when an act was passed legalizing the system in the United States, and directing that it be used in the medical departments of the army and navy and the marine hospital service. In recent years further progress in this direction has been attempted by strong pressure on Congress to pass laws to make the system compulsory, as well as legal. Such a bill did pass the House of Representatives in 1896, but was laid on the table, and since then while a number of metric bills have been introduced at various sessions, no definite action has been taken.

The metric system was based on an absolute unit, and from that absolute unit all other units were directly or indirectly evolved. The standard unit taken was the forty-millionth part of the earth's circumference around the poles, which was called a *"meter."*

This meter was divided into tenths, hundredths, and thousandths, which were called respectively decimeter, centimeter, millimeter. Multiples of the meter were also arranged. A cube, a centimeter each way, was taken as the unit of capacity, and called a *cubic centimeter*. The weight of this cubic centimeter of distilled water at 4° C. (at which temperature water attains its greatest density) was called *gram*, and in this way, from the primal unit of length, the unit of capacity and the unit of weight were obtained.

Of course, denominations other than these three units were essential, and in all cases such units were based on the decimal scale, the change in units of length and the weight being marked by the prefixes deci-, centi-, and milli- (Latin words meaning ten, one hundred, and one thousand), as mentioned above, and deka-, hecto-, kilo- (Greek words meaning ten, one hundred, and one thousand) for the higher units.

An examination of this table of fractions—$\frac{1}{1000}$, $\frac{1}{100}$, and $\frac{1}{10}$—exactly like mills, cents, dimes, and dollars, will show similarity between the metric system and our currency:

10000.	Myriagram.	
1000.	Kilogram.	
100.	Hectogram.	
10.	Dekagram.	
1.	Gram.	Compare this to $1.00 (dollar).
0.10	Decigram.	Compare this to 0.10 (dime).
0.01	Centigram.	Compare this to 0.01 (cent).
0.001	Milligram.	Compare this to 0.001 (mill).

The unit of volume, the cubic centimeter, being very small, one thousand cubic centimeters was adopted as a higher unit and was called a liter; hence, a cubic centimeter is a milliliter, or one-thousandth of a liter. Incidentally, one liter is a cubic decimeter.

Careful measurements have shown that the cubic centimeter has not the same volume as has the thousandth part of the standard liter. While the difference is too trifling to be ordinarily considered, the committee of revision of U.S.P. IX decided to follow the lead of the government scientists and used the word milliliter in place of the term cubic centimeter. In U.S.P. X, however, the term "cubic centimeter" was again employed and it is continued in the U.S.P. XI.

Orthography.—The original French metric terms were "metre, litre, and gramme." These have been anglicized in America into "meter, liter, and gram" and this form of spelling is used in U.S.P. XI.

Of metric weights, we need only consider—

Kilogram, 1000 Gm.
Gm.
Milligram, $\frac{1}{1000}$ Gm. (0.001 Gm.)

The prefixes hecta-, deka-, deci-, etc., should be clearly understood, but in practical work they are not used very often.

The conversion of ordinary weights and measures into the metric or *vice versa* is not so hard as it first seems. All that has to be known is the troy, avoirdupois, and fluid tables and the following facts:

I. That a gram equals 15.5 grains approximately.
II. That a kilogram equals 1000 Gm., and that a milligram is the thousandth part of a gram.
III. That one fluidounce of distilled water weighs, at 77° F., 454.6 grains.
IV. That a cubic centimeter of distilled water weighs 1 Gm. at 4° C.
V. That a liter equals 1000 cc.

With the three tables of weights and measures, given on a preceding page, and the above five facts, any ordinary problem in pharmacopœial weights and measures can be worked.

Just an example or so:

(*a*) How many grams in 4 avoirdupois ounces?
Answer: 1 av. oz. = 437.5 grains.

4 av. oz. = 4 × 437.5 grains = 1750 grains. 1750 grains.

Remember, the denomination "grains" is the bridge across which one passes from the region of the old system to the realm of the metric system.

1 Gm. = 15.5 grains.

Therefore, in 1750 grains there will be as many grams as 15.5 goes into 1750 or 112.9.

```
15.5)1750.00(112.9   Therefore there are about 113 Gm. in 4 avoirdupois ounces.
     155
     ---
      200
      155
      ---
       450
       310
       ---
       1400
       1395
       ----
```

In comparing this example with the tables given by the pharmacopœia it will be found that while the answer just given is 112.9 Gm., the true equivalent is 113.4. This is due to the fact that the exact value of the gram is 15.432 grains.

If 1750 is divided by 15.432, the quotient will be 113.4. However, 15.5 is near enough for most practical pharmaceutic purposes.

(*b*) How many troy ounces in 72.5 Gm.?
Answer: 1 Gm. = 15.5 grains.
72.5 Gm. = 15.5 × 72.5 = 1123.75 grains.

72.5
15.5 1123.75 grains.

3625 We are on the bridge. Now for the other side.
3625
725

1123.75 1 troy ounce = 480 grains.

Therefore, in 1123.75 grains there will be as many troy ounces as 480 goes into 1123.75—

480)1123.75(2.3+
960

1637
1440

So it is seen there are about $2\frac{3}{10}$ troy ounces in 72.5 Gm.

(*c*) How many fluidounces in 120 cc.?
Answer: 1 cc. distilled water at 4° C. = 1 Gm.
1 Gm. = 15.5 grains.
120 cc. distilled water = 120 × 15.5 grains = 1860 grains.

15.5
120

1860.0

Again we are down to *grains*. 1860 *grains*.
1 fluidounce distilled water at 15° C. = 454.6 grains.
Therefore, in 1860 grains distilled water there are as many fluidounces as 454.6 goes into 1860.

454.6)1860.0(4.0+ fluidounces
18184

4160

Hence, in 120 cc. there are somewhat over 4 fluidounces.

(*d*) How many cubic centimeters in 1 pint?
1 pint = 16 fluidounces.
1 fluidounce distilled water = 454.6 grains.
16 fluidounces distilled water = 454.6 × 16 = 7273.6 grains.

454.6
16

7273.6 grains.

Here we are at the crossing! 7273.6 *grains*.
1 cc. distilled water = 15.5 grains.
Therefore, in 7273.6 grains distilled water are as many cubic centimeters as 15.5 goes into 7273.6.

15.5)7273.6(469+
620

1073
930

1436

So it is clear that there are about 470 cc. in one pint.

One other equivalent besides the five already given had better be mentioned.

A gram is 15.5 grains; what then is the value of a *grain* in the metric system? That point is of value in dosage.

The dose of potassium bromide (15–30 grains) is easy to translate into 1 to 2 Gm. But how about strychnine sulfate (dose, $\frac{1}{60}$–$\frac{1}{30}$ grain)?

Here is where the value of a *grain* in *milligrams* is needed.

1 Gm. = 1000 milligrams.
1 Gm. = 15.5 grains.
1 grain = $\frac{10}{155}$ Gm.
Therefore, 1 grain = $\frac{10}{155}$ × 1000 milligrams.

$$\begin{array}{l} 155)10000(64+ \\ 930 \\ \hline 700 \\ 620 \\ \hline \end{array}$$

Accordingly, one grain equals about 65 milligrams, and the dose of strychnine sulfate is 1 to 2 milligrams ($\frac{1}{60}$ × 65; $\frac{1}{30}$ × 65).

1 grain is 65 milligrams or 0.065 Gm.
$\frac{1}{2}$ grain is 32 milligrams or 0.0325 Gm.
$\frac{1}{4}$ grain is 16 milligrams or 0.016 Gm.
$\frac{1}{8}$ grain is 8 milligrams or 0.008 Gm.

The Pharmacopœia (pp. 626 to 636) gives tables for conversion of U. S. into metric units and *vice versa* and accompanying each table is a method of application of the table to a specific official preparation. Liesch has constructed "nomographic" charts permitting the immediate conversion of English into metric units.

WEIGHTS AND MEASURES

The instruments used in the pharmaceutic application of metrology are weights and measures, and the comparison of a given substance to the standard is performed on an instrument called a scale or balance.

The only form of scale with which the mass of a substance is estimated by actual gravity is the *spiral balance,* which consists of a delicate spring to which is attached a scale pan, the elongation of the spiral when a weight is placed in the pan being marked by the descent of an arrow attached to the lower part of the spiral. This needle moves against an index, and the elongation of the spring under influence of gravity can be measured and through this the weight of the body determined (Fig. 1).

The popular modification of the same principle is shown in the common butcher's scale and ice scale.

Pharmaceutic scales are modifications of the principle of a balance which is an application of the well-known mechanical device, the lever. The principle of the lever is very simple, the appliance consisting of a rigid bar and a point (called fulcrum), upon which the bar oscillates; and the power applied in such a way as to raise or otherwise move a weight; this principle being exemplified in the familiar illustration of a crowbar for raising heavy bodies. Acting on the well-known principle that the power applied to raise or move a weight is inversely proportional to the length of the arms of the lever; the longer the arm on which the power is applied, the greater the weight it can raise, and in the same way if the fulcrum is situated exactly midway between the power and the weight, these must be exactly equal to produce a state of equilibrium. On this principle the balance operates, the same primarily consisting of a rigid bar oscillating on a central fulcrum called a knife edge. From either end of the bar are suspended pans on which are placed respectively the power and the weight; the "power" in this case being the standard weight used in determining the quantity of the substance. If the central knife edge is situated exactly midway between the two, a standard weight will be balanced by exactly the same mass of substance desired placed in the other pan; if, on the other hand, the fulcrum is so placed that one arm of the beam is longer than the other, a standard weight placed in the pan suspended from the longer arm will weigh as many times the amount of substance in the pan placed on the short arm as the relative length of the arms.

For the purpose of studying pharmaceutic balances it is convenient to divide them into the following four classes:

Single beam equal arm balances.
Single beam unequal arm balances.
Double beam unequal arm balances.
Compound lever balance.
One arm balance.

SINGLE BEAM EQUAL ARM BALANCES

Several requirements are stated by authorities as essential to a perfect prescription balance, the first being that *the point of suspension should be slightly above the center of gravity.* By the center of gravity is meant the point on which a given object will oscillate absolutely freely: that point at which the weight of an oscillating body is exactly compensated in every direction.

To place the central knife edge exactly at this point is to make the balance so sensitive that time is lost in attempting to bring the beam into a state of rest.

To place the knife edge below the center of gravity means that abnormal condition wherein there is a greater weight above the point of suspension than below, with the result that, at the first opportunity, the heavy part above will endeavor to invert itself.

Second, *the end knife edges should be equidistant from the center, and all three should be on the same plane and parallel to one another.*

It is self evident that if the beam is of exactly the same weight throughout, and an equal arm balance is desired, that condition can be obtained only by having one end knife edge exactly the same distance from the central as the other. As the end knife edges are usually inverted in relation to the central knife edge, the effect of placing these knife edges on the same plane is shown in the appended sketch (Fig. 2).

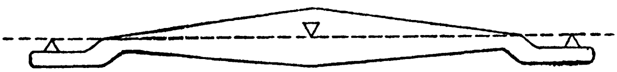


Fig. 2.—Position of knife edges.

Third, *the beam should be of inflexible and light material.*

The lighter the beam, the less friction does it exert on the central knife edge, hence a dictum in successful scale manufacturing is to make the frame as light as possible without sacrificing rigidity.

The knife edges in ordinary prescription balances are of hard polished steel, but as that metal is liable to rust from contact with moist air, and since every particle of rust will increase the friction, rusted knife edges oscillate less freely. In the finer forms of balance this impediment to free oscillation is prevented by making the tips of the knife edges of polished agate, a hard mineral that does not rust.

Not desiring to fill this work with an excess of pictures which can be found in any catalogue of a manufacturer of pharmaceutic apparatus, only typical cases of the several forms of balances will be given.

Testing the Balance.—The testing of a balance to see whether the above requirements are met with is quite a simple matter. Thus, if a scale is sold as being sensitive to a certain weight, say $\frac{1}{100}$ grain, it should show its sensitiveness when such a weight is placed on a scale alone, and also when the scale is burdened with its limit of weight.

If the arms of the balance are exactly equal, the state of equilibrium produced by putting a 100 Gm. weight on either pan should remain the same if these weights are exchanged.

If the knife edges are parallel, moving the weights to various parts of the scale pans will have no effect on the equilibrium of the balance.

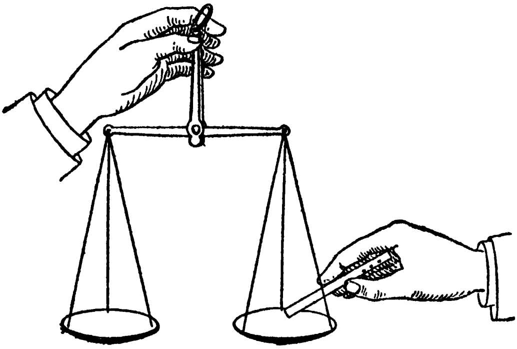


Fig. 3.—Holding hand scale.

Hand Scales.—The simplest form of single beam equal arm balance consists of a beam with pan suspended on either end, the beam itself hanging from a ring held by the hand. In using a hand scale, the ring from which the beam is suspended should be placed on the first finger of the left hand, leaving the thumb and second finger to prevent too great oscillation of the index (Fig. 3).

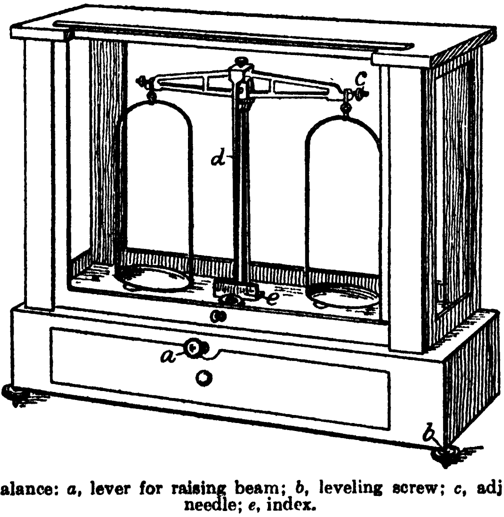


Fig. 4.—Prescription balance: *a*, lever for raising beam; *b*, leveling screw; *c*, adjusting screw; *d*, index needle; *e*, index.

Prescription Balance.—In this balance the beam is not suspended from the hand, but oscillates on a rigid upright column of brass through the center of which passes a rod operated by a lever by which the beam can be raised for oscillation, and lowered in a state of rest, at which time the knife edges are not in contact with the oscillating surface, hence useless friction is avoided. The entire apparatus is inclosed in an appropriate glass case (Fig. 4).

In purchasing a prescription balance it is highly advisable to secure one which has a spirit level and is provided with leveling screws, since to obtain accurate results in weighing it is essential that the balance be perfectly level.

After continued use it will be found that the weight of the two arms may vary, and thus throw the balance out of equilibrium, and to remedy this, the better forms of such balances have a beam on each end of which are buttons which move freely up and down a screw (*adjusting screws*) thus making it easy to attain equilibrium.

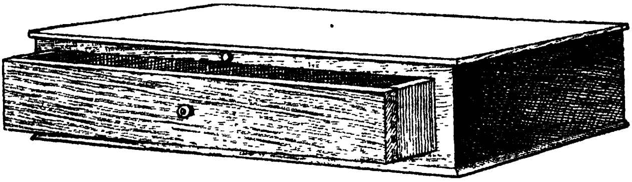


Fig. 5—Army prescription scale (folded).

Attached to the beam near the central knife edge is the metallic needle, which, by its oscillation against the scale, shows when equilibrium is reached. This is attained when the needle, after oscillating, comes to rest at the point on the index directly beneath the point of suspension. To wait until a delicate balance ceases oscillating is a tedious operation, and therefore the pharmacist and chemist often use the method known as reading the zero point, explained under the analytic balanace.

Army prescription balance is a simple and convenient form of single beam equal arm balance, but not of sufficient accuracy to warrant general use in pharmacy. As suggested by the name, it is primarily intended for use by army surgeons and others who move from place to place, being of such manufacture that it can be easily dismantled and carried around in the drawer (Figs. 5 and 6).

Analytic balance is a refined modification of the prescription balance. While the latter is sensitive to $\frac{1}{30}$ grain, the analytic balance is sensitive to $\frac{1}{20}$ milligram, or $\frac{1}{1300}$ grain. In the analytic balance the beam is usually of aluminum, while the knife edges are invariably tipped with agate.

For weighing a smaller quantity than a centigram recourse is had to a rider weight. The rider, which usually weighs a centigram is so shaped as to straddle the beam, and therefore when placed on the beam, exactly over the end knife edge, it will exert the weight of a centigram. The distance on the beam from the end knife edge to the central knife edge is divided exactly into a hundred parts, and up and down the beam on the scale the rider can be moved. Following the principle of the lever, weights which will exert on the opposite scale pan, the force of 1 centigram when placed exactly over the end knife edge, will exert the force of but $\frac{1}{2}$ centigram if moved half way up toward the central knife edge, and will exert the force of but $\frac{1}{10}$ centigram if moved nine tenths of

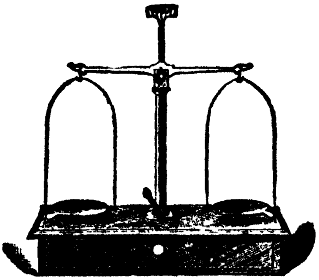


Fig. 6.—Army prescription scale.

the way up toward the central knife edge. The beam being divided into exactly 100 equal parts, the rider can be placed at any of these marks,

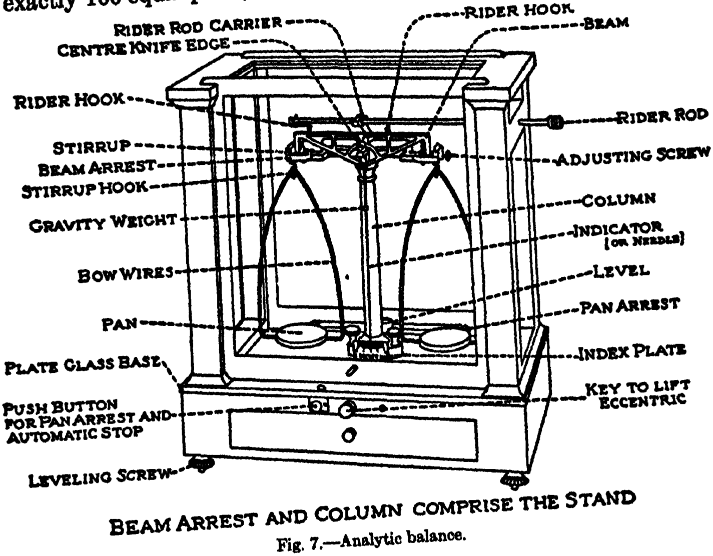


Fig. 7.—Analytic balance.

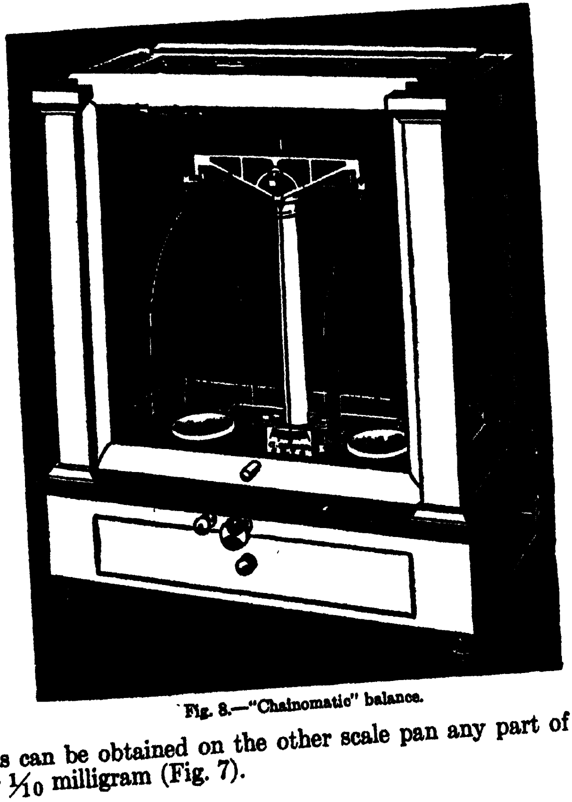


Fig. 8.—"Chainomatic" balance.

and thus can be obtained on the other scale pan any part of 1/100 centigram or 1/10 milligram (Fig. 7).

In the new type *chainomatic balance* (Fig. 8) the rider is replaced by a gold chain (each link of which weighs a milligram) suspended from the beam. As the chain is moved up and down by a rotating device against an upright index, the weight in milligrams and fractions thereof may be ascertained. For extremely accurate work *micrometric balances* are now available (Fig. 9). One form of this balance weighs bodies up to 50 Gm. with the precision of $\frac{1}{10,000}$ of a milligram.

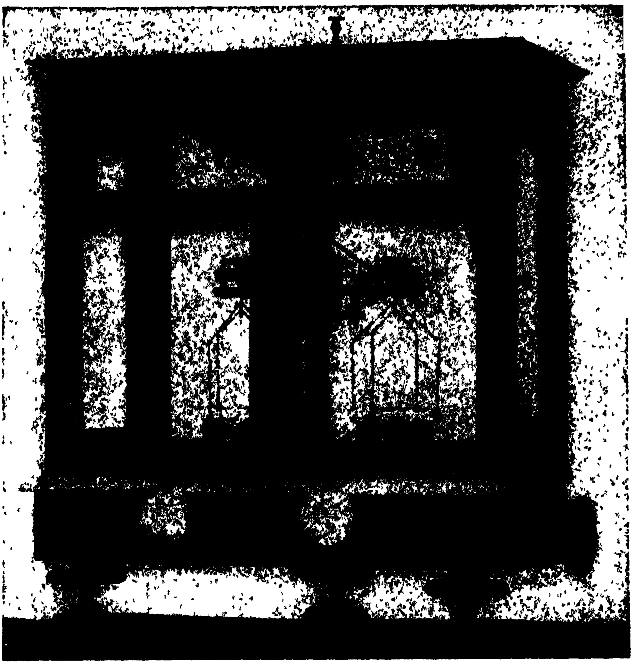


Fig. 9.—Micrometric balance.

Reading Zero.—Time is saved in determining equilibrium by watching the oscillation of the needle against the index mentioned under prescription balances. The index scale on the analytic balance is usually divided into twenty equal lines, ten on either side of the line exactly below the point of suspension.

We set the beam in oscillation, when the needle will move to the left, say five lines, and then, if the beam is in equilibrium, the needle will move back to exactly the fifth line on the right. On the return the needle will go to almost the fifth line to the left. If, however, the index moves to the fifth line to the left and then returns to the second line to the right, it would indicate that the right beam was heavier than the left beam, and equilibrium must be restored by rotating the adjusting screw at the end of that beam.

The careful determination of weight by this means is called "interpolation," full details of which can be found in textbooks on advanced physics.

A large form of single beam equal arm balance is found in the old-fashioned counterbalance shown in Fig. 10.

SINGLE BEAM UNEQUAL ARM BALANCE

In this form of balance the beam, from which is suspended the weight, is usually two to ten times as long as the beam to which is attached the pan on which the substance is to be weighed. Thus the principle of action, as cited above, is that the standard weight is to the substance to be weighed as the length of the short arm is to the length of the long arm. Thus, on such a balance, in which the relative length is one to ten, a weight of 1 pound placed on the end of the long arm exerts a weight of 10 pounds placed at the end of the short arm, and in such balance the weight is usually suspended directly from the beam, which is accurately divided into 100 parts as the beam of the analytic balance, the weight serving in this case the same purpose as the rider in the analytic balance.

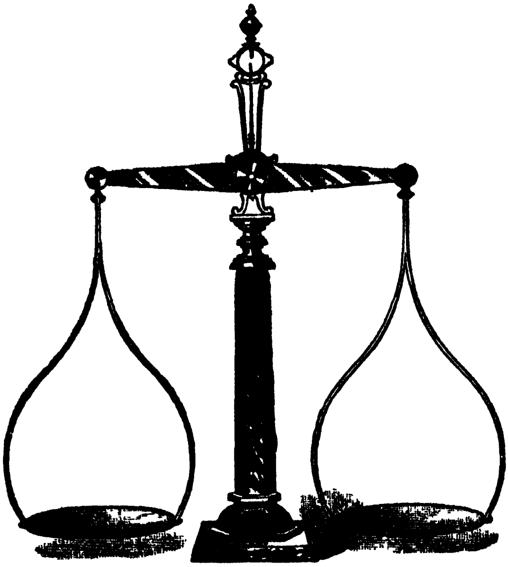


Fig. 10.—Marble counter balance.

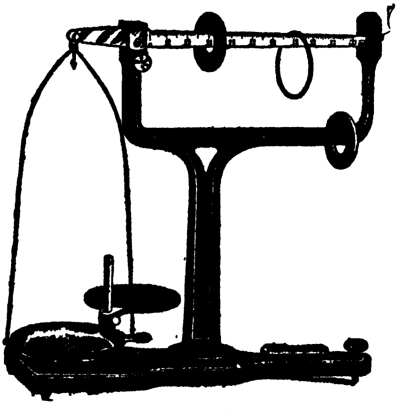


Fig. 11.—Chaslyn balance.

An interesting type of such balance is found in the Chaslyn balance (Fig. 11).

DOUBLE BEAM UNEQUAL ARM BALANCE

This balance is a modification of the preceding one, it being found convenient in many cases to have two beams instead of one, so as to handle two weights. Such a balance is particularly convenient when it is desired to know the tare of a utensil into which the weighed substance is to be placed (Fig. 12).

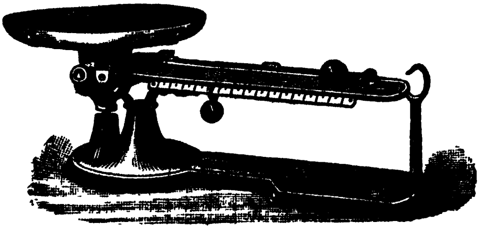


Fig. 12.—Troemner's ball scale.

COMPOUND LEVER BALANCE

In this balance, invented by Roberval (1670), we find a series of levers replacing the single or double beam hitherto discussed, one lever acting on another. The more points of contact, the more the friction, and therefore such forms of balances are, as a rule, less accurate than the single beam; however, they are more durable, and, as a rule, weigh more quickly. Such a form of balance is seen in the usual box counter scale and the box prescription scale (Figs. 13 and 14).

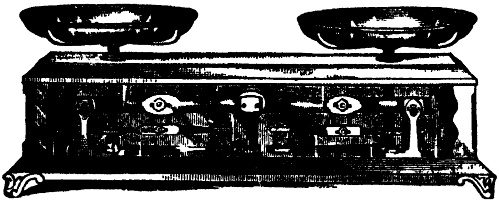


Fig. 13.—Troemner's glass box scale

In both cases the levers are so arranged that a weight placed on a scale is exactly compensated by the same weight on the other beam, hence to all intents and purposes the principle of action is the same as that of the single beam balance.

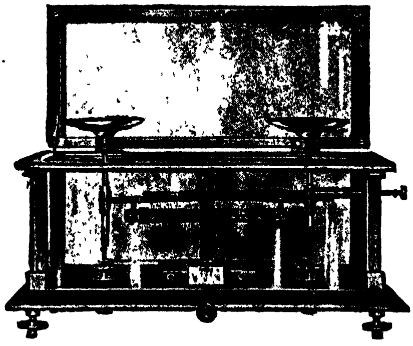


Fig. 14.—Troemner's prescription scale.

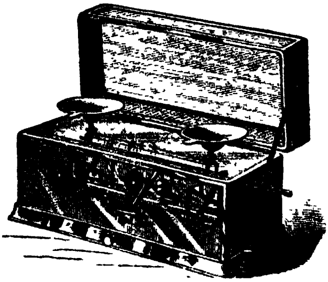


Fig. 15.—Torsion balance.

A modification of the compound lever balance is seen in the ordinary platform scale intended for weighing very heavy articles. In such cases the handling of weight equal to the mass of substance to be weighed would entail vast labor, so such compound lever balances are constructed on the principle of unequal beam balances, consisting primarily of 2 levers, on each

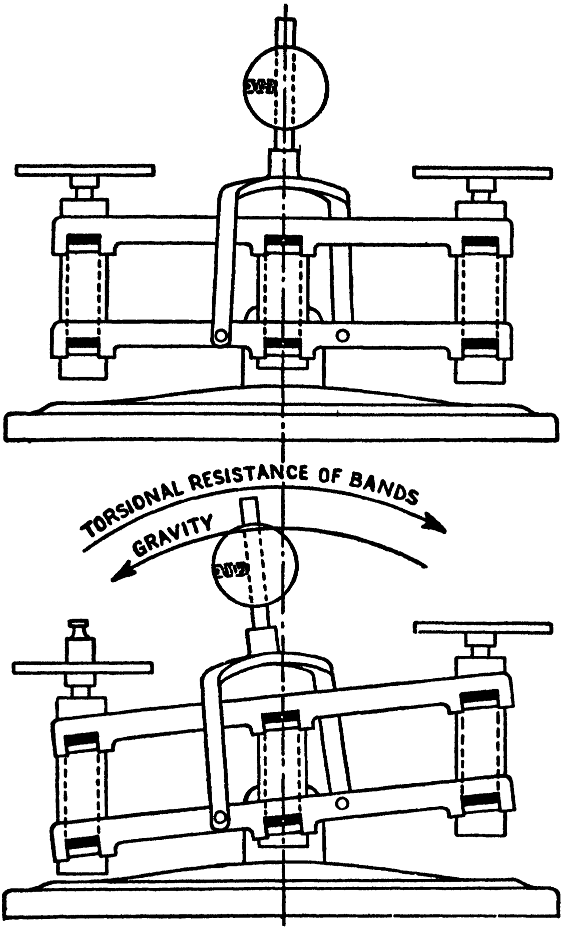


Fig. 16.—Effect of torsion. (Courtesy of Torsion Balance Co.)

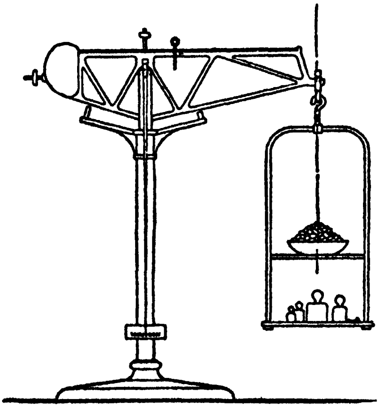


Fig. 17.—Brauer and Reiman one-arm chemical and physical balance.

of which the power is multiplied by 10. In such a balance the weight of 1 pound placed on the first lever exerts on the end of the second lever a force of 10 pounds, and this force of 10 pounds produces a force of 100 pounds on the end of the second lever on which the platform rests; hence on such platform scale a 1-pound weight placed on the end of the index arm will exert the force of 100 pounds on the platform.

One Arm Balance.—This type of balance devised by Brauer and by Reiman can best be described by the following illustration.

The procedure of operation is:

1. Put excess of weights on lower pan and bring to state of equilibrium by adjustment counterpoise on the left of the supporting column.
2. Place object to be weighed on the upper scale pan.
3. Remove weights until equilibrium is restored. These removed weights, of course, represent the weight of the object under observation.

It is claimed that this balance operates with more speed and accuracy than the ordinary two arm balances.

Torsion Balance.—As cited above, the chief objection to steel knife edges is that when they rust, the friction is increased, with a corresponding loss of sensibility. This is obviated by the use of agate knife edges, but that materially increases the cost of the apparatus.

In the torsion balance, knife edges are dispensed with. In the original type, the substitutes were tightly twisted wires through which the beam operated. In modern types the beam is connected with steel frames around which pass tightly drawn steel bands (Fig. 16). The complete balance is found in Fig. 15.

CARE OF THE BALANCE

In the balance we have one of the most accurate physical instruments that has been devised, and also one which, under reasonable treatment, will last many years. In that event, however, due care must be taken to protect the balance from injury, and among the several points which must be enumerated are these:

First, the balance should be kept permanently in a dry room, the temperature of which is as even as possible, and protected from any acid or corroding vapors. In case it is necessary to weigh a fuming liquid, such as nitric acid, it should be placed in a well-stoppered bottle while weighing.

Second, such suggestions as not placing the substance to be weighed directly on the metallic pans, and keeping the pans free from all moisture, seem unnecessary to one who appreciates the value of a balance. Convenient for accomplishing these results are the movable glass scale pans which can be purchased from any scale manufacturer.

Third, weights should never be left on the balance, and, whenever possible, should be transferred to the balance by means of pincers.

Fourth, under no circumstances should the balance be left to oscillate after weighing is finished, and during the weighing it should be brought to a state of rest whenever new weights or new portions of the substance being weighed is placed thereon.

WEIGHTS

The weights used on scales and balances are composed of iron, brass, or aluminum, and of such shape as convenience suggests. Thus, the cheap avoirdupois weights are made of iron, while those finer are composed of brass, and the more expensive are nickel plated, and their shapes are usually those shown in Fig. 18.

The troy weights are usually made in sets nested, each weight, therefore, being a cup inclosing all the weights of smaller denominations than itself, the smallest, usually ¼ troy ounce, being solid, and fitting in a cup-shaped weight of the same denomination (Fig. 19).

As the avoirdupois weights, so the metric are composed of iron or brass; fine analytic metric weights are sometimes gold-plated brass and are sometimes platinum coated.

In purchasing avoirdupois and metric weights it is usually wisest to choose such as are arranged in a block. A very convenient form of such block is made of cast iron, the objection to wooden blocks being that they frequently swell, rendering it difficult to remove the weights.

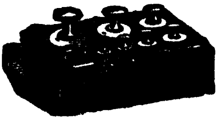


Fig. 18.—Brass block weights

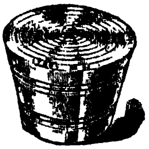


Fig. 19.—Troy cup weights (solid brass).

The metric analytic weights should be in a fine wooden box, the depressions in which the weights rest being lined with velvet, serving the double purpose of keeping the weights from being scratched and preventing them being held fast by the swelling of the wood. The denominations under 1 Gm. are made of sheet platinum.

For dispensing purposes troy weights are used, the denominations under 10 grains being made of aluminum, either in sheets or in the form of wire, the latter being bent into as many sides as the weights have grains.

MEASURES

In pharmacy the larger measures, gallons, quarts, etc., are not often used, although reliable measures of these sizes should be found in every well-regulated pharmacy. These are made of brass, tinned iron, or enameled iron.

Indispensable in the prescription department are graduates or measures, from a pint down, made of glass, with the subdivisions of the unit marked on the sides (Fig. 20). The graduation of these measures is performed in two ways: in one the plunger used in making the utensils out of the molten glass is graduated; thus the finished graduate is produced in one operation. More accurate, however, are those in which the graduating is done by hand, the quantity of liquid being poured into the ungraduated vessel from a burette, and this quantity of liquid is carefully marked, the finishing of the graduate being done by the engraver.

The subdivisions of graduations are into drachms and minims in ordinary graduates, and into cubic centimeters in the metric.

The minim graduate, however, is far from being reliable as a large amount of the liquid is retained by capillarity of the glass vessel, and, therefore, for measuring minute quantities, a pipette should be used. Such pipettes, graduated to minims, were put on the market by Dr. E. R. Squibb (Fig. 21), and are more reliable not merely by reason of the dispensing of the full quantity of the liquid, but, being narrower than a graduate of equal capacity, there is less chance for error in pouring more or less of the liquid into the utensil; the narrower the graduate, the more accurate can the quantity desired be determined.

In this way, for delicate analytic work, a liter graduate is rarely used, there being substituted for it a flask of such size that when filled with a liter of water the water rises within the narrow neck of the flask. Such a liter flask is used chiefly in volumetric analysis, liquids being delivered and measured from same by means of pipettes (Fig. 23) and by burettes (Fig. 24).

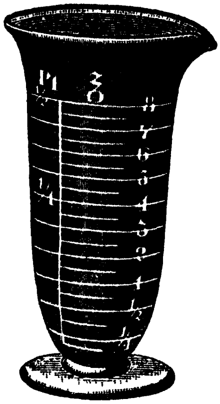


Fig. 20.—Eight-ounce graduate.

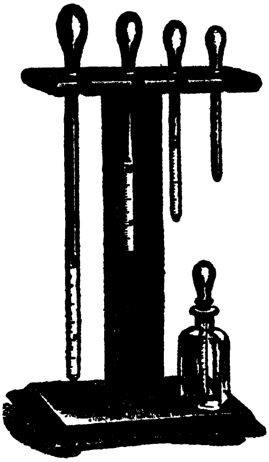


Fig. 21.—Squibb's minim pipettes.

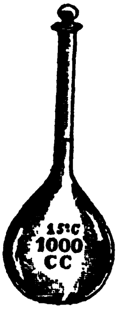


Fig. 22.—Liter flask.

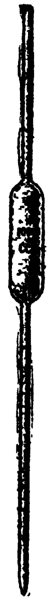


Fig. 23.—Volumetric pipette.

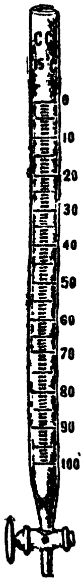


Fig. 24.—Burette.

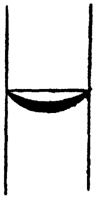


Fig. 25.—Meniscus (Sollmann).

In both cases the liquid is measured within a narrow tube, hence based on the same principle as the liter flask (Fig. 22).

In placing liquids in a comparatively small utensil, like a burette, it will be observed that, through capillarity, the liquid is attracted to the sides of the vessel, thus making an edge which it is sometimes difficult to read; such an edge is called a "meniscus," and reading the quantity of the liquid, the line representing the quantity should be exactly at the bottom of the meniscus.

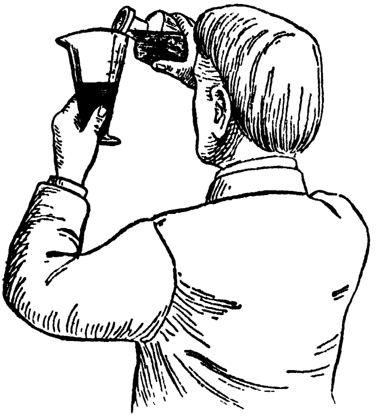


Fig. 26.—Pouring into graduate.

Lloyd has given careful study to the subject of menisci. The meniscus is of importance not only in correctly reading the volume of a liquid in a graduate, measuring cylinder or burette, but is also of great scientific interest in studying the line of contact between immiscible liquids. Professor Lloyd also studied from the purely physical standpoint the formation of drops and bubbles at the interface between two liquids. For details, see the three papers cited in the bibliography at the end of this chapter.

It is hardly necessary to state that in measuring liquids in a graduate the latter should be held perfectly level and the line representing the desired quantity even with the eye (Fig. 26).

BIBLIOGRAPHY

Weights.—(History) J. Q. Adams, Report on Weights and Measures, 1821; Ellis, A.J.P., 2, 1830, 111; Arny, Am. Dr., 42, 1903, 250 and 282; Anon, Dr., Circ., 58, 1914, 111; Nichols, A.J.P., 101, 1929, 307. (Grain) Lloyd, A.Ph.A., 43, 1895, 137. (Avoirdupois drachm) Sturmer, Dr. Circ., 59, 1915, 727. (Gallon) Mason, Am. Dr., 17, 1888, 2; Lyons, Am. Dr., 17, 1888, 41. (Size of drops) Payne, Dr. Circ., 41, 1897, 125; Eschbaum, Nat. Dr., 39, 1909, 19; Lohnstein, Z. physik. Ch. through C.A., 8, 1914, 1041; Morgan and co-workers, Jl. Am. Ch. Soc., 35, 1913, 1821, 1834 and 1845.

Metric System (General) Arny, Sci. Monthly, 4, 1917, 207; Pract. Dr., 35, Apr., 1917, 23; A.J.P., 89, 1917, 175; Modern Hosp., 9, 1917, 174; Jl. A.Ph.A., 6, 1917, 254 and 7, 1918, 280 and 1052; Barton, Measurement, 6, July, 1931, 7. (Liter) De Baillehache, C.A., 8, 1914, 2284. (Milliter *vs* "cc.") Stutt, Jl. Frank. Inst., 208, 1929, 829. (Teaspoon) Arny, Jl. A.Ph.A., 6, 1917, 1056.

Balances and Weighing.—Brandel and Kremers, The Balance; Benton, Jl. Soc. Ch. Ind., 46, 1927, 741 and 764; Cocking, *ibid.*, 50, 1931, 696; Karrer, Jl. Ind. Eng. Chem. Anal. Ed., 3, 1931, 112. (Ultrabalance) Waag, Umschau, through C.A., 20, 1926, 1151; Holtz, C.A., 20, 1926, 214.

Metric Conversions.—Liesche, Chem. Fab. through Jl. Soc. Ch. Ind., 48, 1929, 305B and 495B.

Interpolation and Analytical Weighing.—Dayton Miller, Laboratory Physics, 1903, 57; Wells, Jl. Am. Ch. Soc., 42, 1920, 411.

Measuring Fluids.—Andrews, Jl. A.Ph.A., 24, 1935, 477.

Standard Pipette.—Traube, Ph. Zt., 54, 1909, 203.

Graduate Making.—Parrish, A.Ph.A., 10, 1862, 199; Pilé, A.Ph.A., 21, 1873, 573.

Menisci and Drops.—Lloyd, Jl. A.Ph.A., 11, 1922, 409; Lloyd, Ostwald and Haller, *ibid.*, 18, 1929, 862 and 20, 1931, 95.

CHAPTER III

SPECIFIC GRAVITY

In Chapter II care was taken to mention that 454.6 grains was the weight of a fluidounce of distilled water. Why distilled water? Would it not be the weight of a fluidounce of chloroform as well? Common sense teaches that "some liquids are heavier than others," as we put it—that chloroform is heavier than water. A fluidounce of chloroform weighs about 670 grains, against 454.6 grains, the weight of the same volume of water. Accordingly, we see that chloroform is nearly one and one-half times heavier than water. That gives the idea of specific gravity, the definition of which can be given as *the relative weight of equal bulks of different bodies*, adding thereto the provision that, for solids and liquids, the unit of specific gravity is distilled water.

Now, to go back to our chloroform example: the volume, the bulk, the capacity of that 1-ounce graduate remains the same whether it contains water or chloroform. Therefore a fluidounce—be it of water or of chloroform—represents "equal bulk." The respective weights of a fluidounce of the two liquids is "relative weight," and, reducing to unity, the specific gravity is obtained.

Instead of the term "specific gravity," the word "density" is the more happy choice, since the term "specific gravity" suggests the gravitating force of the earth, which has only indirect connection with the subject.

The estimation of the specific gravity of various substances is of value, first, as the indication of purity or strength of the substance, and, second, through the data thus afforded we can determine the volume of the substance, while in a minor degree it is sometimes of service in the diagnosis of disease.

The first application of density given above can be best explained by a simple illustration, thus: the average 93 per cent sulfuric acid has a specific gravity of about 1.84; in other words, is 1.84 times heavier than water. If this acid is mixed with water, the density of the liquid will vary to somewhere between 1.84 and 1.00, and, indeed, varies in proportion to the amount of water added.

In the same way official 92.3 per cent alcohol has a specific gravity of 0.810 at 25° C. and is, therefore, 0.8 times as heavy as water. If such alcohol be mixed with water, the specific gravity of the liquid will rise to some point between 0.810 and 1.000, and, indeed, in proportion to the amount of water added; hence by taking the specific gravity of such liquid, we can determine the exact strength of the liquid. Tables of this character have been carefully worked out, and are found in the Pharmacopœia.

The other two uses of specific gravity, being of lesser importance, will be discussed elsewhere in this book.

Determination of the density of a body differs according as the substance is solid or liquid, and since, by the explanation given above, the specific gravity of liquids becomes simple, we will first discuss the determination of the specific gravity of liquids; afterward, that of solids.

There are several ways of determination of the specific gravity of liquids: (*a*) by use of pyknometer or specific gravity bottle; (*b*) with the hydrometer; (*c*) with the Mohr-Westphal balance; (*d*) with Lovi's beads; (*e*) with the Jolly spiral balance.

DETERMINATION OF SPECIFIC GRAVITY OF LIQUIDS

With the Pyknometer.—As mentioned above, the determination of the specific gravity of a liquid is rendered simple because of the ease with which the weight of a bulk of given liquid can be compared to the weight of an equal bulk of water. Thus, in the simplest methods of estimation all that is necessary is to determine the weight of a fluidounce of water in a graduate, then pour out the water, dry the graduate, pouring in the same measure of the liquid, the specific gravity of which is desired, weighing same, and then comparing the weight of the fluidounce of water with the weight of the fluidounce of liquid. As many times heavier as is the weight of the fluidounce of the liquid than the weight of the fluidounce of water, so many times heavier is that liquid than water, which figure represents the specific gravity. The inaccuracies of this method of estimation are due to the same causes as any inaccuracy in the measurement of liquids by means of the graduate, as mentioned in the preceding chapter, viz., the uncertainty in reading an exact volume of a liquid when placed in as wide a vessel as a graduate; hence, we generally weigh the liquid, the weight of which is to be compared to the weight of an equal bulk of water, in a flask called a *pyknometer*, two modifications of which are shown in Figs. 27 and 28.

The only advantage a pyknometer (or specific gravity bottle) has over the graduate method just given is its greater accuracy. By tilting a graduate in measuring it is very easy to get a little more or a little less than the quantity desired, and every grain counts in estimating specific gravity.

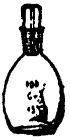


Fig. 27.—Pyknometer.

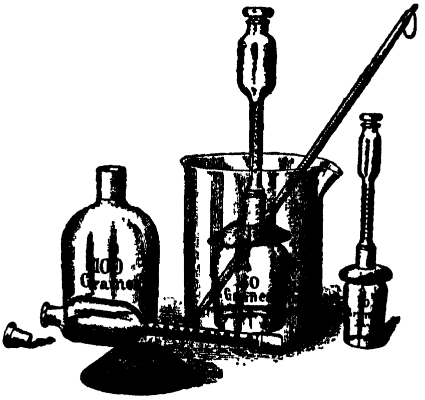


Fig. 28.—Squibb's pyknometer.

In glancing at the narrow neck of the pyknometer it can be seen how the danger of incorrect readings is lessened. Then, too, the pyknometers usually hold 1000 grains or 100 Gm., which renders long division unnecessary. If a 1000-grain bottle holds 1500 grains of a certain liquid, it is obvious that the specific gravity of that liquid is 1.50.

In both cases the possible variation in the volume of the liquid when manipulated by a person of ordinary intelligence is practically nil.

The method of determining specific gravity by means of the pyknometer is by all odds the most accurate means at our disposal, but the process is one requiring considerable time. To facilitate more rapid reading other instruments have been devised, most useful of which is the *hydrometer*.

The Hydrometer.—As to the principle of a hydrometer, if asked in which fluid one could float better, in fresh or in salt water, the instant answer would be in salt water. Why? Simply because salt water, being heavier, buoys one up more. And, following the rule, the heavier the liquid, the more it will buoy a body up, and, indeed, proportionally. To prove this it may be cited that while a piece of iron will sink in water, on mercury it will float around like a chip in water. Why? Simply because while iron is eight times heavier than water, mercury is thirteen times heavier, and the lighter iron will float on the heavier mercury.

The hydrometer consists of a glass tube at the base of which 2 bulbs are blown, one containing enough shot or mercury to enable it to hold an upright position when immersed in water, and the other and upper one filled with air (Fig. 29). According to the theorem of Archimedes, a body when immersed in water loses as much weight as the weight of the water it displaces, that is, a body displaces its own weight of a liquid and, accordingly, as the liquid is lighter or heavier than water, so does the hydrometer sink or rise when immersed in same.

There are two classes of hydrometers, in one of which the weight of the hydrometer remains the same, whereas the point at which it floats varies accordingly as the liquid is lighter or heavier, and the other form, which is designed to float always at the same point in a liquid, which feat is accomplished by weighting down the hydrometer when immersed in a heavy liquid, *i. e.*, by meeting the buoyancy of the heavy liquid by adding weights in a pan at the top of a floating instrument.

Of the first class, we have such well-known hydrometers as Baumé's and Daniel's, while on the principle of the second type are based the Nicholson, Fahrenheit, and the Mohr specific gravity balance.

Baumé's Hydrometer.—The sketch and explanation given above explain the construction of the above-named hydrometer, except details as to its graduation.

In constructing the hydrometer, it was early noted that such an instrument designed to measure accurately the specific gravity of the commonly known liquids, ranging, say, from ether (0.713) to bromine (3.000), would of necessity be so long as to be inconvenient.

Baumé, at the outset, made two forms of this hydrometer, one for liquids heavier than water, and one for liquids lighter than water. The one for heavier liquids is graduated by weighting same with sufficient shot so that it would be almost completely immersed in water, and the point which was in contact with the surface of the water was marked or denominated zero. He then immersed this instrument in a 15 per cent solution of common salt, whereupon, by reason of the superior buoyant force of this liquid over water, the hydrometer was pushed up and the point of contact of the hydrometer with the surface of the salt solution was marked off and denominated 15, and the space between the zero mark and 15 accurately divided into 15 spaces (provided always that the circumference of the tube was the same all along its length).

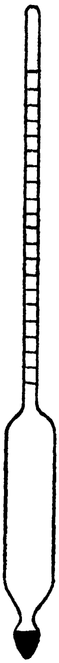


Fig. 29.—Hydrometer (schematic).

The remainder of the tube was divided into spaces equal to the 15 spaces between the water contact and the solution of salt contact, and this marking was arbitrarily denominated "degrees Baumé heavy."

In a similar manner was the hydrometer for lighter liquids constructed, this hydrometer being weighted so as to float in a 10 per cent solution of salt at a point very near the base of the tube, and this point was marked zero.

It was then floated in water, when it naturally sank, and the place of contact with the surface of the water was marked 10, and the spaces between the water contact and the salt contact divided into 10 equal spaces, which spacing was continued up to the length of the tube, and in turn designated "degrees Baumé light."

While the original hydrometers were thus constructed at present they are standardized by dipping the hydrometer in water and then into a standard liquid (concentrated sulfuric acid for the "heavy" hydrometer; ether for the "light" one), marking the floating point, the "degree Baumé" corresponding to the specific gravity of the standard liquid, and then subdividing the space between the floating point in water, and in the standard liquid into the number of uniform spaces equal to the difference in "degrees," water and the standard liquid.

This description shows how exceedingly arbitrary and confusing was the Baumé marking, for not only have we "degrees" which in themselves signify nothing, but we have "degrees Baumé light" and "degrees Baumé heavy." Thus, when the statement is made that the specific gravity of the liquid is 15° Baumé, the first thing that we must find out is whether a light or a heavy hydrometer was used. Most unfortunate is it that this Baumé marking is largely used in commerce, where heavy chemicals are bought and sold by degrees Baumé rather than by their actual specific gravity.

It therefore behooves every retail pharmacist to be able to convert degrees Baumé into specific gravity rapidly, which can be easily done by using the following factors:

To convert heavy degrees Baumé into specific gravity:

$$\frac{145}{145 - {}^\circ\text{B.}} = \text{sp. gr.}$$

Thus 20° Baumé heavy =

$$\frac{145}{145 - 20} \text{ or } \frac{145}{125} \text{ or } 1.16.$$

To convert light degrees Baumé into specific gravity, use the following factors:

$$\frac{140}{130 + {}^\circ\text{B.}} = \text{sp. gr.}$$

Thus 20° Baumé light =

$$\frac{140}{130 + 20} = \frac{140}{150} = 0.933.$$

Aside from these general features of the hydrometer we find modifications of the hydrometer especially adapted for taking the specific gravity of certain liquids; thus we have the *alcoholometer* for estimating the strength of alcohol through the specific gravity. Usually, the marking of this form of hydrometer is not in terms of specific gravity, but in the actual percentage of alcohol. In the same way we have the *lactometer* for estimating the strength and density of milk; the *saccharimeter* for estimating density of syrups; and the *urinometer* for estimating the density of urine.

Urine differs in specific gravity from 1.010 to 1.070, and since the instrument is very small, the marking is from 10 to 70 instead of the actual specific gravity, as stated above.

The best form of urinometer shown in Fig. 30 was devised by Dr. E. R. Squibb.

Nicholson's Hydrometer.—This apparatus is of scientific interest because its principle of action differs from that of the hydrometers just considered by being arranged to operate at a constant level, but with varying weight. Such a hydrometer has but one mark on tube, and is made to float in all liquids at this point by adding or taking away weights from the pan, as shown in Fig. 31.

On account of the inconvenience of using it, this hydrometer is practically limited to lecture counter demonstration, though at least two modifications of the same principle are found in very useful forms of specific gravity apparatus.

The first of these is *Rousseau's densimeter*, shown in Fig. 32, in which the scale pan of the Nicholson hydrometer is replaced by a small cup, and into this cup is poured the liquid the specific gravity of which is desired, while the instrument itself is floated in water. From the depth to which the standard amount of liquid sinks the hydrometer, the specific gravity of the liquid can be deduced. The prime value of Rousseau's densimeter is to take the specific gravity of liquids which are either very costly or so rare that a larger quantity, such as is necessary for a pyknometer or a hydrometer, is not obtainable.

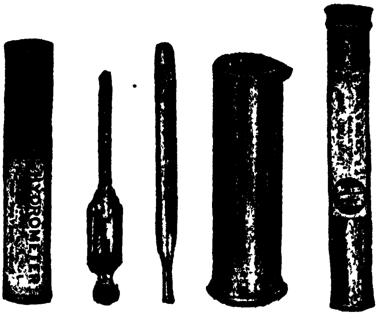


Fig. 30.—Squibb's urinometer.

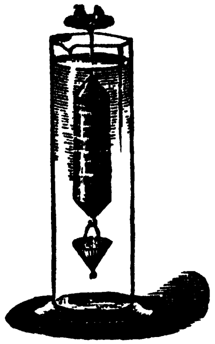


Fig. 31.—Nicholson's hydrometer.

The Mohr-Westphal Balance.—In this balance as in the Nicholson hydrometer, the principle of operation is the floating of weighted cylinder. In the case of the Westphal balance, however, the floating cylinder is permanently attached to the end of the scale beam, and a constant level maintained by keeping the balance in equilibrium. In making such a balance a cylinder is made out of small glass tube weighted with an appropriate quantity of mercury (or else a thermometer), and the exact bulk of same is carefully determined by immersing same in water contained in a burette or other narrow graduated tube, and noting the rise of the water when the cylinder or thermometer is completely immersed (Fig. 33).

This cylinder is suspended from one end of the beam, the other end of which is weighted so as to produce equilibrium in air. When the cylinder is immersed in water, the buoyancy of the latter throws the balance out of equilibrium, which, however, can be restored by placing on the beam, directly over the knife edge from which the cylinder is suspended, an appropriate weight in the form of a rider; this weight must, of course, be exactly that of the weight of the bulk of water, equal to the bulk of the cylinder, for the body immersed in water loses as much weight as the weight of the water displaced.

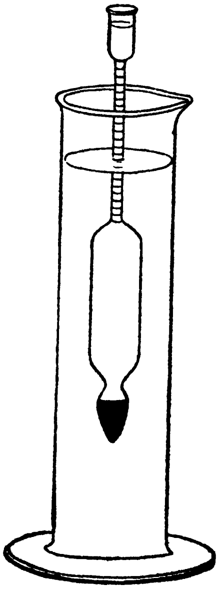


Fig. 32.—Rousseau densimeter.

In the Westphal balance the beam is accurately divided into ten equal parts, up and down which the rider can be freely moved. Duplicate of this rider weight is also provided, and likewise two weights, one tenth and one one-hundredth the value of the original rider weight. By means of these rider weights the specific gravity of any liquid can be accurately determined. Thus, in the picture one large rider is on the notch over the point of suspension, meaning specific gravity 1.000. The second large rider is on the notch 2 of the beam, corresponding to specific gravity 0.200. The one-tenth weight rider is on notch 5, corresponding to specific gravity 0.05; while the one one-hundredth weight rider is on notch 7, corresponding to specific gravity 0.007. These four weights, therefore, show that the specific gravity of the liquid is 1.257.

Lovi's Beads.—Lovi's beads are one of the simplest forms of hydrometers. They consist of beads of glass so weighted with mercury that a definite proportion exists between the weight of the bead and its volume. Thus, a bead measuring 2 cc., if weighted with mercury enough to weigh exactly 3 Gm., will be one and one-half times heavier than water, since 2 cc. of water weighs 2 Gm.

A bead having the capacity of 2 cc. and weighing 2½ Gm. would be one and one-fourth times heavier than water. A bead having a capacity of 2 cc. and containing enough mercury to weigh 1½ Gm. would be three fourths as heavy as water, or have a specific gravity of 0.75, and, lastly, a bead of 2 cc., containing enough mercury to weigh exactly 2 Gm., would be the same weight as water, or specific gravity 1.000.

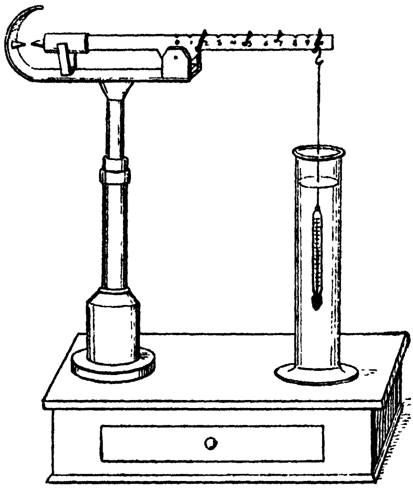


Fig. 33.—Mohr-Westphal balance.

After getting their weights accurately adjusted, the beads are sealed and the specific gravities marked on the outside thereof.

If these four beads were thrown into water, the one having specific gravity 0.75, being lighter than the water, would float thereon, and the ones of the specific gravities 1.50 and 1.25 would sink, being heavier than the water, while the one of exactly the same specific gravity as the water would float indifferently at any place in the water where immersed. In the same way, if these beads were thrown into a liquid of specific gravity 1.25, the bead marked 1.50 would sink, those of specific gravities 0.75 and 1.00 would float on the surface of the liquid, while the one of specific gravity 1.25 would float indifferently.

Thus are Lovi's beads employed, a handful of them being thrown into the liquid the specific gravity of which is to be ascertained, and the one which floats indifferently in the solution is of necessity of the same specific gravity as the liquid.

The application of such beads is usually limited to the estimation of specific gravity of boiling liquids, in some processes of manufacture it being directed that the liquid be evaporated to a certain specific gravity. If in such a heated liquid a hydrometer is placed, there is more danger of fracture than if Lovi's beads were applied.

Jolly's Spiral Balance.—This balance, described on p. 39, can be used instead of the ordinary balance for estimating specific gravity of either solids or liquids. In the case of solids, the weight of same is ascertained in air and then in water and the well-known rule applied: weight in air divided by loss of weight in water equals specific gravity.

In case of determining specific gravity of liquids, a sinker whose volume is known is suspended from the balance, and its downward force, its weight, is determined in air, in water, and in the liquid whose specific gravity is desired to be known. In this way we learn the loss of weight of the sinker in water and in the liquid, and from these data the specific gravity of the liquid in question is deduced.

DETERMINATION OF SPECIFIC GRAVITY OF SOLIDS

The specific gravity of solids can be determined in several ways: (*a*) by means of graduated tube; (*b*) by floating in liquid of known specific gravity; (*c*) by means of a hydrostatic balance; (*d*) with a pyknometer.

With Graduated Tube.—Specific gravity is the weight of a substance compared to the weight of an equal bulk of water, and, as cited above, the determination of the weight of a certain bulk of liquid and comparison of this to the weight of an equal bulk of water means the simple expedient of weighing a certain volume of the liquid and comparing it to the weight of the same volume of water. Taking the specific gravity of a solid is rendered more difficult by reason of the fact that the great majority of masses of solids possess irregular surfaces, making the exact measurement of their cubical capacity an impossible task, while the lack of mobility of their particles, which distinguishes the solid from the liquid, prevents solid masses from assuming the shape of a standard vessel. Hence the weighing of a certain bulk of solid, for comparison with an equal bulk of water, by means of a pyknometer alone, is out of the question. The only method, therefore, of determining the volume of the substance as compared to the volume of water is by immersing the solid in the water contained in a graduated tube and noting the rise of the water upon immersion. Thus, if a piece of brass weighing 8 Gm. immersed in water contained in a burette causes the surface of that water to rise 1 cc., it will mean that 1 cc. of this brass weighs 8 Gm. We know that 1 cc. of water weighs 1 Gm., and if the brass weighs 8 Gm., its specific gravity must be 8.

By Immersing Solid in Liquid of Known Specific Gravity.—We have already learned, under Lovi's beads, that a substance weighing the same as the same bulk of a certain fluid will float indifferently in that fluid, and this principle was used to estimate the specific gravity of a liquid by throwing beads of known specific gravity therein. Inversely, the specific gravity of a solid can be determined by throwing the solid into liquids of different specific gravities, and noting in which liquid the substance floats, in which it sinks, and, above all, in which it floats indifferently. Thus, if a piece of ore sinks in a solution of mercuric nitrate of specific gravity 2.00 and floats in a solution of potassio-mercuric iodide of specific gravity 3.00, it can be safely assumed that this ore has a specific gravity somewhere between these two figures, and the exact specific gravity can be ascertained by diluting the last solution with sufficient water until the ore floats indifferently therein, then noting the specific gravity of the liquid by means of the hydrometer.

Such method of determination is of comparatively limited application, by reason of its lack of convenience, and an accurate determination by this method takes more time than does the well-known process of weighing in air and then in water. Its chief use, therefore, is limited to mineralogic work, in which case a series of solutions of known specific gravities, ranging from 1½ to 3, are kept constantly on hand, and the determination of the gravity of the selected ore made by throwing same into one solution, then into another, until we find the solution in which it floats indifferently.

A pharmaceutic application of this method was suggested by Hager for determining the specific gravity of wax, he preparing a series of ten strengths of diluted alcohol of specific gravities ranging from 0.950 to 0.970, and the freshly melted drop of wax is thrown into one after the other of these solutions. A modification of this method is used for wax in the present Pharmacopœia.

The two methods of determination of specific gravity just given are of little pharmaceutic value, and are cited first merely because they give the principles of density more clearly than the method in general use; that determination being—

By Means of a Hydrostatic Balance.—In taking the specific gravity of solids by this process four conditions are possible:

First, the solid may be insoluble in, and heavier than, water.

Second, the solid may be insoluble in, and lighter than, water.

Third, the solid may be soluble in, and heavier than, water.

Fourth, the solid may be soluble in, and lighter than, water.

(A) *Solids Insoluble in and Heavier than Water.*—As mentioned above, the direct comparison of the bulk of a mass of solid with the same bulk of water is a matter of some difficulty. Some indirect method had to be devised, and this is reached by a practical application of a theorem of Archimedes, one of the ancient philosophers.

Suppose, into a glass full of water to the brim, an 8-ounce brass weight is dropped; of course, the water will overflow. Now, Archimedes found an interesting comparison between the weight of the overflowing water and the changed weight of the brass in the water. He found that a body in water weighed less than it did in air. The student should demonstrate this for himself, for practical demonstrations are of great value. Take a hand scale and tie a weight beneath the pan; weigh it in the air, then in the water, when it will be found that brass, which weighs 8 ounces in air, weighs only 7 ounces in water. Therefore the brass is said to "lose" 1 ounce of its weight when immersed in water.

Archimedes showed that the amount of water displaced from the full glass mentioned above was 1 ounce in weight also. Accordingly, he devised his famous theorem, "A body immersed in water loses as much weight as the weight of the water it displaces." Naturally, the amount of water displaced by a body means a bulk equal to that body, and thus we indirectly get the weights of equal bulks of water and the body with which we are experimenting. If the relative weights of equal bulks of water and some other liquid were as 1 is to 8, the specific gravity of the other liquid would be 8 divided by 1, or 8; if the relative weights were, say, 240 grains for water, and 480 grains for the other liquid, the specific gravity of the latter would be 480 divided by 240, or 2. Remember that loss of weight of a body in water means the weight of a bulk of water equal to that of the body, and one can easily understand the rule for taking the specific gravity of solids. "Weigh the body in air, then in water. Divide the weight in air by the loss of weight in water, and the quotient will be the specific gravity."

The principle of this case has been considered, but as to practical manipulation, it need only be stated that the substance of which the specific gravity is desired is attached to a balance by a fine silk thread, better, a horsehair, suspended in a beaker, or other suitable glass containing distilled water of definite temperature (usually 15° C.), after being carefully weighed in air.

It will be observed that the body weighs less in water than it did in air, and the difference between these two figures (the loss of weight in water) is, according to the theorem of Archimedes, exactly the same as the weight of the same bulk of water; hence if an 8-Gm. brass weight immersed in water weighs 7 Gm., the loss of weight of 1 Gm. can be transcribed into the statement that the quantity of water of exactly the same bulk as the 8-Gm. weight would weigh exactly 1 Gm.

If, during this experiment, the brass weight is immersed in a graduated tube, it will be found that, on placing the 8-Gm. brass weight below the surface of the water, the water in the tube will rise exactly 1 cc. if the temperature of the water is 4° C. Now, 1 cc. of water weighs 1 Gm., and, therefore, we learn that the loss in weight in water of a given substance is exactly equal to the weight of an equal bulk of water.

This being the case, we see that, by determining the loss of weight in water, we have a direct comparison of the weight of the substance with the weight of an equal bulk of water, and all that is necessary in order to deduce the specific gravity is to divide the weight in air by the loss of weight in water, that is, divide the weight in air by the weight of an equal bulk of water, it being always remembered that the specific gravity means how many times heavier a substance is than is the same bulk of water. Hence, memorize this rule: *weight in air, divided by loss of weight in water, equals specific gravity.*

(B) *Solids Insoluble and Lighter than Water.*—Such solid of necessity floats on the surface of the water, and in order to find the loss of weight in water the substance must be completely immersed. In determining the specific gravity of such solids they must be forced under the surface of the water by attaching some heavy substance, for example a brass weight.

The method of taking the specific gravity of the substance after immersion is practically the same as that of taking the specific gravity of a solid insoluble in and heavier than water, namely: we must know the weight of the substance and the sinker separately in air, the weight of both in water, and the weight of the sinker alone in water.

The weight of the two substances, minus the weight of both in water, gives the loss of both in water, and from this figure the loss of the weight of the sinker alone is taken; we then have the loss of weight of the lighter substance in water, whereupon we apply the rule: *weight in air divided by loss of weight in water equals specific gravity.*

An illustration of such an estimation is as follows: a piece of wax weighs 4 Gm. in air, and to immerse same, we attach a brass weight weighing 50 Gm. The two weigh in water 43.84 Gm.; hence the loss of the weight of the two in water equals 54 − 43.84, or 10.16 Gm.

Then we immerse the sinker in water and find it weighs 44 Gm. Then the weight of the sinker in air (50 Gm.), minus the weight of the sinker in water (44 Gm.), equals the loss of weight of the sinker in water (6 Gm.). The combined loss of weight (10.16 Gm.) minus the loss of the sinker alone (6 Gm.) gives the loss of the weight of wax in water (4.16 Gm.). The weight of the wax in air (4 Gm.), divided by the loss of the weight in water (4.16 Gm.), gives the specific gravity (0.960).

In observing these figures, the student is confronted with what, at a first glance, seems a peculiar statement, that a piece of wax weighing 4 Gm. loses, when immersed in water, 4.16 Gm.; that is, it loses more weight than it actually possessed. This can be easily explained, however, when we appreciate the fact that weight is merely the measure of the gravitating force of the earth, and that when a substance hanging toward the earth is immersed in a liquid, it is acted upon by an opposing upward force, namely, the buoyant force of water. This explains why, when a substance is immersed in water, it is said to lose weight, the so-called "loss of weight" being the difference between the actual attractive force of the earth and that same force when modified by the upward force of the liquid in which the substance is immersed.

In case of solids lighter than water the upward buoyant force of the liquid is greater than the downward force of gravitation, hence the phenomenon of a body losing more weight than it originally possessed.

(C) *Solids Soluble in and Heavier than Water.*—It is hardly necessary to state that with some substances (lump sugar, for example) we cannot accurately determine the loss of the weight in water, for while we are endeavoring to weigh the substance in water, the water will be dissolving the solid, which will finally disappear under the solvent action of the liquid; in such cases, therefore, we must have recourse to an indirect determination, namely: by determining the loss of weight of the substance in some liquid in which it is insoluble, and, from this, determining what would be the loss of weight of the same substance in water by a proportion involving the respective specific gravities of the two liquids.

Thus, if a piece of alum weighs in air 3 Gm., and weighs in turpentine (sp. gr. 0.87) 1.48 Gm., the loss of weight in turpentine will be 1.52 Gm. If we divide the weight in air by the loss of weight in turpentine, we would estimate how many times heavier the substance was than turpentine, which datum is of no interest to the observer. In other words, the loss of weight in turpentine represents the weight of an equal bulk of turpentine, while what we really want to know is the weight of an equal bulk of water (or loss of weight in water).

This is determined by the following proportion:

The specific gravity of turpentine is to specific gravity of water as the loss of weight in turpentine is to the loss of weight in water, and applying this to the above example, we have:

$$0.87 : 1.00 :: 1.52 : x$$

$$x = \frac{1.00 \times 1.52}{0.87} = 1.74.$$

By this we see that the piece of alum, which lost 1.52 Gm. in turpentine, would lose 1.74 Gm. if it were possible to estimate the loss of weight in water by immersing same therein. This obtained, we apply the usual rule:

Weight in air divided by loss of weight in water equals specific gravity, and get—$3.00 \div 1.74 = 1.73$. (Specific gravity of the alum.)

(D) *Solids Soluble in and Lighter than Water.*—Of this comparatively rare class of bodies it need only be said that the determination of the specific gravity of same is carried on by combining the two previous methods of determination, viz., to the substance we attach a weight or sinker and immerse same in some liquid in which it is insoluble; in this way we have a double determination to perform: first, to subtract the loss of weight of the sinker from the combined loss of weight, as in (B). Take the loss of weight of the substance alone in the liquid, and deduce therefrom the loss of weight in water, as in (C). Lastly, apply the rule: *weight in air divided by loss of weight in water equals specific gravity.*

With the Pyknometer.—The determination of specific gravity of solids by means of the balance is limited to such substances possessing sufficient cohesion to enable same to be suspended from a thread or horsehair, a method which is inapplicable to powders.

In determining the specific gravity of powders, therefore, recourse is had to a modification of the pyknometer experiment, which can be best explained by citing a possible case.

Assuming we had powdered calomel weighing 10 Gm., we would take the specific gravity of same in a pyknometer, holding, say, 100 Gm. distilled water. Now, if all the 100 Gm. of water would remain in the pyknometer on the addition of calomel, the combined weight would be, of course, 110 Gm. However, it is an accepted fact that when the powdered calomel is placed in a bottle, water will be displaced and some rejected, the amount of rejected water being equal to the weight of an equal bulk of calomel. In the actual experiment the weight of the 10 Gm. of calomel and of water sufficient to fill the 100-Gm. bottle was found to be 108.6 Gm. This shows that the amount of water displaced is 110 − 108.6, or 1.4 Gm. In other words, the weight of a bulk of water equal to the bulk of the 10 Gm. calomel was 1.4 Gm.; hence the calomel is as many times as heavy as water as 1.4 goes into 10; hence the specific gravity of the calomel is $10 \div 1.4$, or 7.1.

As mentioned on p. 59, the knowledge of the specific gravity of pharmaceutic substances aids us in estimating the volume of a certain weight of liquid.

Thus, if we know that the specific gravity of sulfuric acid is 1.83, and we have a recipe calling for a given weight of same, we can transcribe this weight into the liquid volume of the acid by dividing the number of grams directed by the specific gravity of the acid. In the same way if we wish to know what size container is necessary to hold 20 avoirdupois pounds of glycerin (sp. gr. 1.25), we can find out by a simple calculation involving the number of gallons in 20 pounds of water and dividing this number by the specific gravity of glycerin. This latter example, however, is perhaps more properly solved by specific volume, mention of which will be made shortly.

In answer to the question as to the chemicals of which we should study the specific gravities, it might be stated that every pharmacist should know at least the following average densities:

Ether	0.716
Chloroform	1.475
Glycerin	1.249
Alcohol	0.810
Sulfuric acid	1.840
Nitric acid	1.403
Mercury	13.500

These figures represent the specific gravity of each substance at 25° C. (77° F.), for bear in mind that temperature is an important factor in deducing specific gravity—the higher the temperature, the less dense the liquid.

A practical demonstration of the use of specific gravity may be valuable. We want to know how many grains there are in a fluidounce of ether, specific gravity 0.716.

One fluidounce of distilled water weighs 454.6 grains; therefore a fluidounce of ether, sp. gr. 0.716 weighs 454.6 × 0.716 or 325.49 grains.

SPECIFIC VOLUME

Specific volume is just the inverse of specific gravity.

Specific gravity is the relative weight of equal bulks of different bodies.

Specific volume is the relative bulk of equal weights of different bodies.

To get the specific volume of a body we divide 1.000 by the specific gravity. Thus, the specific volume of chloroform is approximately 0.666+:

$$1.000 \div 1.50 = 0.666+.$$

As a homely example, while specific gravity means, in a general way, how many avoirdupois ounces, grams, etc., in 1 pint, liter, etc., of alcohol, chloroform, etc., specific volume teaches what size bottle it will take to hold a pound or a kilogram of the substance in question. Thus specific gravity deals with what weight of a certain substance will go into a certain sized bottle, while specific volume asks what sized bottle will hold a certain weight of the substance. If we say chloroform has the specific gravity 1.50, we mean (since pint and avoirdupois pound of water are somewhat approximate) that a pint of chloroform weighs somewhere around 1½ avoirdupois pounds. Regarding this same chloroform, an avoirdupois pound of it will not, as is full well known, fill a pint bottle. In fact, it will easily go into a 12-fluidounce bottle. We get nearer its exact bulk by dividing 16 by the specific gravity, or, in the present case, 16 divided by 1.50 equals 10.6, and we find that 1 avoirdupois pound of chloroform has a bulk of about 10.6 fluidounces. This is only approximate, for, in truth, a pint of water weighs more than an avoirdupois pound, and, again, the specific gravity of chloroform is 1.475 (at 25° C.), not 1.50. The exact determination of the weight of a pint and the volume of an avoirdupois pound of chloroform is as follows:

1 pint = 16 fluidounces.
1 fluidounce distilled water = 454.6 grains.
1 pint (16 fluidounces) distilled water = 454.6 grains × 16 = 7273.6 grains.
16 fluidounces chloroform (sp. gr. 1.475) = 7273.6 × 1.475 = 10,728.56 grains.
7000 grains = 1 avoirdupois pound.

Therefore, in 10,728.56 grains there are as many avoirdupois pounds as 7000 goes into 10,728.56:

$$10{,}728.56 \div 7000 = 1.532,$$

and we see that 1 pint of chloroform weighs 1.532 avoirdupois pounds, considerably over 1½ avoirdupois pounds. Now for the volume of 1 avoirdupois pound of chloroform:

1.532 avoirdupois pounds of chloroform measure 16 fluidounces.
1 avoirdupois pound of chloroform will measure $^{1000}/_{1532} \times 16 = 10.4$ ounces.

LABORATORY EXERCISES

SPECIFIC GRAVITY OF LIQUIDS

Determine specific gravity as follows:

Take a 1-ounce graduate and carefully tare it. "Tare" means to counterbalance it—to put on the other scale just enough weights so that it will be exactly balanced.

Now, very carefully measure into it exactly one fluidounce of water (distilled, if possible) and note how many grains the water weighs.

Then weigh in similar manner 1 fluidounce of alcohol. Determine its specific gravity by comparison of its weight with the weight of the fluidounce of water, and then looking in the back of the Pharmacopœia or dispensatory, find the table showing alcoholic strength according to specific gravity (commonly called alcohol table), and deduce from the specific gravity what the strength of the alcohol is.

Lastly, find the weight of a fluidounce of glycerin and work out its specific gravity from this weight, remembering always that specific gravity is the relative weight of a body as compared to the weight of an equal bulk of water.

Then do same work more accurately by means of pyknometer. (See p. 60.) The necessary data to be obtained are as follows:

Water.—Weight of pyknometer ____________________
Weight of pyknometer filled with water ____________________
A. Weight of *water* held by pyknometer ____________________
Alcohol.—Weight of pyknometer ____________________
Weight of pyknometer filled with alcohol ____________________
B. Weight of *alcohol* held by pyknometer ____________________
Glycerin.—Weight of pyknometer ____________________
Weight of pyknometer filled with glycerin ____________________
C. Weight of *glycerin* held by pyknometer ____________________

Calculations.—Since the same pyknometer is used in each case, and since specific gravity means how many times heavier than water is a certain substance, we find the specific gravity of alcohol by dividing weight of alcohol by weight of same volume water:

B ÷ A = sp. gr. of alcohol;
________ ÷ ________ = ______________;

and we find the specific gravity of glycerin by dividing its weight by weight of same volume of water.

C ÷ A = sp. gr. of glycerin.
________ + ________ = ______________.

Oil of Turpentine.—Lastly, fill pyknometer with oil of turpentine, and from the weight of turpentine deduce the specific gravity of that liquid, viz.:

Weight of turpentine in pyknometer + weight of water in pyknometer = specific gravity. (How many times the oil of turpentine is heavier than water.)

____________________ + ____________________ = ____________________

Be sure to wash the pyknometer carefully after the turpentine experiment until free from the odor of that oil.

Remarks.—In weighing, give value to centigrams.

Use *distilled* water in all specific gravity experiments. In weighing the empty pyknometer, be sure it is absolutely dry (wipe it with clean handkerchief) both inside and out.

In filling it with any liquid be sure to have no air bubbles in the liquid and to have it completely filled up to top of capillary orifice in stopper. The latter is accomplished by filling almost to top of neck of pyknometer, and then suddenly and evenly plunging the stopper into the neck. The excess of liquid passes through capillary to top of stopper, and is carefully wiped off with a piece of filter paper. The entire pyknometer is then carefully wiped with a clean handkerchief and then weighed.

After wiping the top of the stopper of the pyknometer, the heat of hand may cause expansion of liquid, which will rise through capillary to top of stopper. Do not wipe off this excess, but weigh it on top of stopper.

After weighing, empty out liquid and carefully wash out pyknometer with water (and alcohol if necessary), and dry perfectly before filling with another liquid. Water, if present, will contaminate the other liquid.

In accurate work the temperature at which pyknometer is filled should be noted, and, if possible, the liquid should be at 25° C.

SPECIFIC GRAVITY OF LIQUIDS WITH HYDROMETER

Take three tall cylinders and fill about three quarters—the first with water, the second with alcohol, the third with glycerin.

Take two hydrometers (p. 61), one for heavy liquids, the other for light liquids, and note to which degree the hydrometer sinks in each liquid—the line just appearing at the surface of liquid.

	Degrees light	*Degrees heavy*
Water		
Alcohol		
Glycerin		

These are "degrees Baumé," and calculate therefrom by process given on p. 62 the specific gravity of each liquid. From the specific gravity of the alcohol deduce by means of alcohol table given in the pharmacopœia its alcoholic percentage.

Remarks.—Be sure that each cylinder is perfectly clean and dry before pouring liquids in, so that each liquid can be returned to container after the determinations, absolutely pure. In the same way carefully clean and dry each hydrometer before transferring to another liquid.

Avoid air bubbles in putting hydrometers into liquids, as air is lighter than the liquids and air bubbles vitiate results.

As the principle of the action of the hydrometer is fully explained on p. 61, nothing but the actual operation is here given.

With Alcoholometer.—Take very tall cylinder—a long narrow percolator with cork in neck does quite nicely at a pinch—and fill about nine tenths with alcohol. Sink therein the alcoholometer (p. 62) and note point at which it floats. Note the two scales on the alcoholometer—one the alcoholic percentage, the other, its value in "proof." For "proof" valuation see p. 658.

With Lovi's Beads.—Throw a handful of Lovi's beads into water in a pint graduate. Some will sink, some will float on surface, and perhaps one will float midway in liquid. Take out those on the surface and all will be found to have specific gravity less than water; those which have sunk have specific gravity greater than water, while the one floating will be the specific gravity of water. Carefully dry and repeat with any other liquid if desired.

With Mohr's Balance.—Take Mohr's balance (p. 63) and note that the sinker in air is exactly counterpoised by weight on other end. Put water into cylinder, and immerse sinker therein. Note that the buoyant force of the water presses sinker upward. Place largest weight on notch directly over place from which sinker is suspended, when equilibrium will be restored. If desired, the *volume* of the sinker can be measured by sinking it into water contained in a burette and noting rise of water; the *weight* of weight which restores equilibrium may then be taken, in which event it will be found that the *volume* of the sinker, expressed in cubic centimeters, is just the same as number of grams be that the weight weighs.

Having brought the balance into equilibrium by placing weight in notch over point of suspension, take sinker out of water, dry, and immerse in alcohol. It will then be found that the weight and sinker are heavier than the buoyant force of the alcohol.

Move weight to next notch toward middle of beam (nine tenths the distance between central knife edge and point of suspension of sinker). It will still be too heavy. Move to next notch (eight tenths the total distance). That will be a trifle too light, showing that the alcohol is something over eight tenths as heavy as water (over sp. gr. 0.800). Use the two smaller weights—one one tenth as heavy as the first, the other one tenth as heavy as the second. The number of notch on which the second will all but produce equilibrium will give the second decimal point of the specific gravity (thus if it all but balances on notch No. 2, the specific gravity will be 0.820). Then, with the third weight, bring balance to perfect equilibrium, and use this notch number as the third decimal point place.

Immerse dried sinker into *glycerin,* and weigh as before. It will be found that this liquid will buoy up the beam even when the heaviest weight is placed in the notch directly over the point of suspension of the sinker; that the buoyant force of glycerin is greater than that of water. Therefore, leaving the heaviest weight on the notch over point of suspension of sinker, where it represents the specific gravity 1.000, take the mate to the heaviest weight and place it on the notch where it most nearly balances the beam—if, when on notch three, it is too heavy, then put it on notch two, and if this is a trifle too light, consider the specific gravity as 1.20, and fill out the second and third weights on the appropriate notches as in the alcohol experiment. In this way deduce the specific gravity of glycerin.

Specific Gravity of Solids.—As learned on p. 65 the two important methods of taking the specific gravity of solids are, first, comparing the weight of a solid to the weight of an equal volume of water, and, second, by dividing weight in air by loss of weight of the solid in water. In the latter case we divide by *loss of weight in water* because, according to the Archimedes theorem (p. 66), loss of weight in water equals the weight of water displaced when the body is immersed in water; also equals the weight of a bulk of water equal to the bulk of body immersed.

The first part of the following work is given in the hope of proving the Archimedes theorem to the student:

1. Take 20-Gm. brass weight and weigh in air with other weights to prove it is 20 Gm.

Then take test tube and half fill it with water, marking water level by a scratch with a file or with a piece of string or rubber band. Then sink therein the 20-Gm. brass weight, to which a silk thread is attached. The water will rise, the amount displaced being, of course, exactly equal to the bulk (the volume) of the weight. Mark point to which water rises as the original level of water was marked. Then remove weight carefully, bring water in test tube to original level if any is lost in removing weight, and pour in water from graduate to highest mark, and thus measure in cubic centimeters the amount of water displaced.

Since 1 cc. of distilled water weighs 1 Gm. we can put down—

20-Gm. brass weight displaces____cc. water.
has same volume as____cc. water.
has same volume as____Gm. water.

Since specific gravity is telling how many times heavier a substance is than the same bulk of water, we can deduce the specific gravity of the brass thus:

Weight of brass (20 Gm.) ÷ Weight of same volume of water = Sp. gr. of brass.

Now, take same brass weight, hang to the hook from which the scale of the balance is suspended, immerse in water contained in a beaker held independent of the hanging scale pan, and weigh immersed in water.

As in the experiment with the Mohr's balance, it will be seen that the brass weighs less in water than in air, due to the buoyant force of the water. Weight in air minus weight in water equals *loss of weight in water.*

If the operation is conducted with care, it will be found that the *loss of weight of brass in water is exactly the same as the weight of the water displaced* in the previous experiment, thus proving the Archimedes theorem. Lastly, the loss of weight in water equals the weight of an equal bulk of water, hence, when more convenient, instead of finding the weight of an equal bulk of water by the test-tube experiment, we can weigh the substance in water and deduce specific gravity as follows:

Weight brass in air ÷ Loss weight brass in water = Sp. gr. of brass.

Specific Gravity of Wax.—To determine the specific gravity of a body by "loss of weight in water," the substance must be completely immersed. Wax and many other substances float on water, and to get the specific gravity of such a body, it has to be forced beneath the surface of water by means of an appropriate weight, say the 20-Gm. weight of the preceding experiment. The loss in weight of such a sinker under water then enters into the calculation, rendering it somewhat more difficult, as the following data must be taken:

Weight of wax in air.................................. ______ Gm.
Weight of 20 Gm. brass weight in air.. .... ______ Gm.

Weight of both together in air......................... ______ Gm.
Weight of both together in water....................... ______ Gm.

Loss of weight of both together in water .... ______ Gm.
Loss of weight of brass alone in water................... ______ Gm.
Loss of weight of wax alone in water..................... ______ Gm.

Then apply rule:

Weight of wax in air ÷ Loss of weight of wax in water = Sp. gr. of wax.

Remarks.—In performing this experiment, the wax must be firmly attached to the silk thread by which the brass weight is suspended, and both immersed well under water, as in the foregoing experiment. In all cases of this kind great care must be exercised in removing all air bubbles from the immersed solids, as such bubbles render the solids more buoyant, and hence vitiate the results.

When wax data are worked out, there will be noticed what seems at first an astonishing fact—*that the wax loses more weight in water than it actually possessed in air.* This can, however, be understood if we remember that weight is a purely relative state; that it represents the downward force of the earth's gravitation exerted on a solid with naught but the air to interpose. On the other hand, when immersed in water, the buoyant force of that liquid—the repelling force of its molecules—pushes the solids *up* the same time that gravitation is drawing it *down.*

In the case of solids lighter than water, the upward force of the water is greater than the downward force of the earth; hence the "loss of weight in water" is greater than "the weight in air."

Specific Gravity of Alum.—Many solids dissolve in water, and these cannot be weighed in water, hence in such cases the specific gravity of such solids must be determined by weighing the solid in some liquid in which it will not dissolve. In this case we employ the oil of turpentine, the specific gravity of wnich has just been taken with the pyknometer.

The alum suspended by silk thread is weighed in air, then is immersed in a beaker containing oil of turpentine, and weighed, when we get the following data:

Weight of alum in air................................. ______ Gm.
Weight of alum in turpentine.......................... ______ Gm.
Loss of weight of alum in turpentine.................. ______ Gm.

If we divide the weight of the alum in air by its loss of weight in turpentine, we find how many times heavier it is than oil of turpentine. This we do not care to know; what we want to know is, how many times heavier it is than water; hence we must indirectly estimate what the loss of weight of the alum would be in water. This we can figure out by the following proportion:

$$\left\{\begin{matrix}\text{as the sp. gr.}\\ \text{of turpentine}\end{matrix}\right\} \text{ is } \left\{\begin{matrix}\text{to the sp. gr.}\\ \text{of water}\end{matrix}\right\} \text{ so } \left\{\begin{matrix}\text{the loss of weight}\\ \text{in turpentine}\end{matrix}\right\} \text{ is } \left\{\begin{matrix}\text{to the loss of}\\ \text{weight in water}\end{matrix}\right\}$$

$$\begin{matrix}\underline{\qquad\qquad} & : & 1\ 000 & : & \underline{\qquad\qquad} & : & x\\ \text{a} & & \text{b} & & \text{c} & & \end{matrix}$$

$$x = \frac{\text{b} \times \text{c}}{\text{a}}$$

Having thus deduced loss of weight of alum in water, we estimate its specific gravity by the regular rule:

Weight in air of alum ÷ Loss of weight in water = Sp. gr. of alum.

Before closing this chapter, other phases of simple arithmetic as applied in pharmacy may be well taken up.

ALLIGATION

Alligation, or "the rule of mixtures" as applied in pharmacy, includes those arithmetical processes used in ascertaining the relative amount of different strengths of the same substance needed to blend into a substance of a definite intermediate strength. Thus, by alligation we solve such problems as the blending of two strengths of opium into a third strength.

Opium, as we will learn later, is a substance whose activity is based on the amount of morphine it contains, and when we say 10 per cent opium, we mean that 100 Gm. of the drug contain 10 Gm. morphine; by 18 per cent opium we mean one that contains 18 Gm. morphine to each 100 Gm.; while 14 per cent opium is such as contains 14 Gm. to the hundred. It can be seen that we can combine 10 per cent opium and 18 per cent opium to make 14 per cent opium, nor is it difficult to figure out that equal quantities of 10 per cent and 18 per cent will make 14 per cent; but upon what principle is the arithmetic calculation based?

The best comparison of alligation is with the principle of the balance, as fully explained on p. 46. What do we mean by a single equal arm balance? It means a beam represented by the line *a–b* (Fig. 34) of the same weight throughout, suspended on a central knife edge, with pans hanging from the end knife edges (*a* and *b* respectively). In order that the balance swing exactly even it is necessary that the central knife edge, *c*, be exactly midway between *a* and *b*. Thus, if we call *a* 10 inches, and *b* 18 inches, the beam would be 18 − 10, or 8 inches long, and if *c* be at 14 inches, it will stand 18 − 14, or 4 inches, from *b*, and 14 − 10, or 4 inches, from *a*, and 4 pounds placed on pan *a* would be exactly balanced by 4 pounds placed on pan *b*.

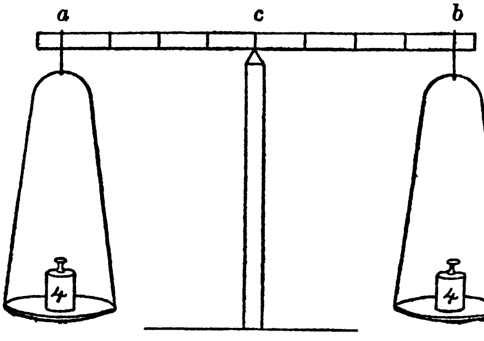
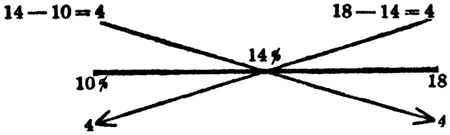


Fig. 34.—Alligation I.

Compare this to the following opium alligation. We have 10 and 18 per cent opiums and wish to mix them so as to make 14 per cent. This we solve as follows:



And we see that 4 pounds of 10 per cent and 4 pounds of 18 per cent give 8 pounds of 14 per cent.

Again, what do we mean by a single beam unequal arm balance? We mean a beam, like Fig. 34, only with knife edge *c* *not* midway between *a* and *b* (Fig. 35).

Assuming as before that we call *a* 10 inches and *b* 18 inches, we would have a beam 8 inches long, and if *c* were at 12 inches, it would stand 18 − 12, or 6 inches, from *b*, and 12 − 10, or 2 inches, from *a*. In order to balance such a beam different weights must be placed on pans *a* and *b*, following the general principles of the lever; namely, a certain weight placed on the pan of the long arm *b* will exert an increased power on the weight in the pan of the short arm *a*, and in direct proportion to the length of the arms. Thus, in Fig. 35 the long arm *b–c* (6 inches) is 3 times longer than the short arm *a–c* (2 inches); hence 1 pound placed on pan *b* will balance 3 pounds placed on pan *a*, or 2 pounds in pan *b* will balance 6 pounds in pan *a*. Compare this to the following opium alligation. We have 10 and 18 per cent opiums and desire to mix them so as to make 12 per cent. This is solved as follows:

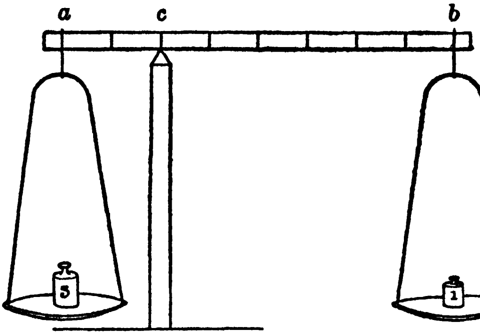
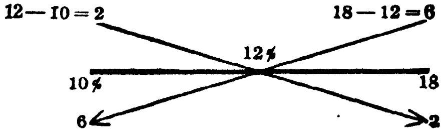


Fig. 35.—Alligation II.



And we see that 6 pounds of 10 per cent and 2 pounds of 18 per cent give 8 pounds of 12 per cent.

Likewise, assuming our beam has different dimensions, as follows: *a*, 9 inches; *b*, 14 inches; *c*, 12 inches. The beam will then be 14 – 9, or 5 inches long, and *c* being 12 – 9, or 3 inches from *a*, and 14 – 12, or 2 inches, from *b*, then the weight of 3 pounds placed on pan *b* (14 inches) will be balanced by 2 pounds placed on pan *a* (9 inches).

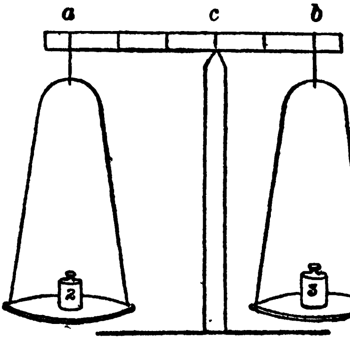
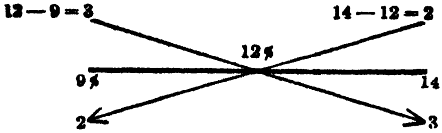


Fig. 36.—Alligation III.

Compare this to the following alligation:

We have 9 and 14 per cent opiums and want to make 12 per cent. This we solve below:



And we see that 2 pounds of 9 per cent and 3 pounds of 14 per cent give 5 pounds of 12 per cent.

Thus, can every problem in alligation be solved, and when we draw our line, with the percentage wanted, above, and the percentages we have, below, like this—

12
9 14

we are unconsciously comparing the matter to a single beam balance. A purely arithmetic solution of alligation is the following tiresome but lucid process.

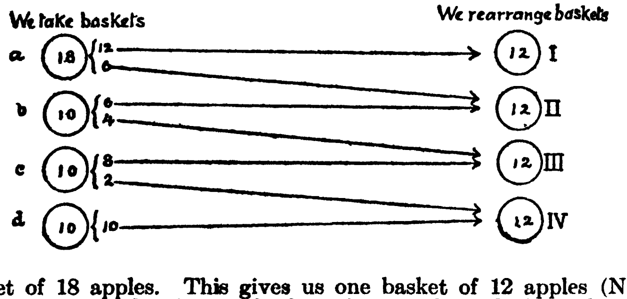
Suppose we take the problem given above: How much 10 and 18 per cent opiums are needed to make 12 per cent?

10 per cent opium means 10 parts morphine to 100 parts opium
18 " " " " 18 " " " 100 " "
12 " " " " 12 " " " 100 " "

These figures are exactly analogous to:

10 apples in a basket
18 " " " "
12 " " " "

and as if the question were, How many baskets of 10 apples each and 18 apples each must be taken to arrange baskets containing 12 apples each? Let us do the actual rearranging:



One basket of 18 apples. This gives us one basket of 12 apples (No. 1) and 6 apples over. These 6 and 6 from a basket of 10 apples, which we bring here, will make another basket of 12 apples (No. II). Six apples from 10 leaves 4 apples in our basket *b* and, bringing up basket *c* (10 apples) we take out 8, making basket No. III contain 12 apples. This leaves 2 apples in basket *c*, which, plus 10 apples from basket *d* makes 12 apples to put into basket IV, and the trick is done.

The conclusion is that 1 basket of 18 apples and 3 baskets of 10 apples each give 4 baskets of 12 apples each; the same result as the similar alligation, which showed that—

6 pounds of 10 per cent (or 3 pounds of 10 per cent)
and 2 pounds of 18 " " (or 1 pound of 18 per cent)
give 8 pounds of 12 " " (or 4 pounds of 12 per cent).

The algebraic solution of alligation problems is as follows:

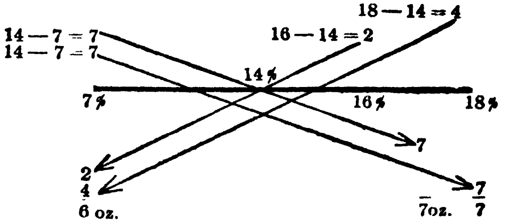
Let x represent quantity of the lowest percentage used.
Let y " " " " highest percentage used.
Let z " " " " percentage desired.

Then the problem, How much 10 and 18 per cent opiums are needed to make 12 per cent? is solved as follows:

$10x + 18y = 12z. \quad z = x + y.$
$10x + 18y = 12x + 12y.$
$18y - 12y = 12x - 10x.$
$6y = 2x. \quad x = 3y.$

Then, if $x + y = 4$ pounds, and $x = 3y$, $3y + y = 4$ pounds, or $4y = 4$ pounds.
$x = 3y. \quad y = 1$ pound. $x = 3$ pounds.
Hence, 3 pounds 10 per cent
and 1 pound 18 per cent
give 4 pounds 12 per cent.

If the problem involves three different percentages, say, 7 per cent, 16 per cent, and 18 per cent, out of which to make another percentage, say, 14 per cent, the calculation is accomplished by means of the mechanic "rule of the balance" explained above, viz.,



That is: 6 ounces of 7 per cent opium
7 " " 16 " " "
7 " " 18 " " "
make 20 ounces of 14 per cent opium.

And if the problem was to make 14 per cent opium from 5 per cent, 15 per cent, 16 per cent,, and 18 per cent opium, the calculation would be as follows:

14 − 5 = 9. This goes under 15 per cent, 16 per cent, and 18 per cent
15 − 14 = 1. This goes under 5 per cent
16 − 14 = 2. This goes under 5 per cent
18 − 14 = 4. This goes under 5 per cent

14 per cent			
5 per cent	15 per cent	16 per cent	18 per cent
1	9	9	9
2			
4			
7	9	9	9

That is: 7 ounces of 5 per cent opium
9 " " 15 " " "
9 " " 16 " " "
9 " " 18 " " "
make 34 ounces of 14 per cent.

In explanation of the fact that in the examples furnished above we find two, and in the other case three, separate quantities of lower percentage which must be added to the stronger, let it be said that the example can be considered as three separate examples or problems, viz.:

(A) How much 5 per cent and 15 per cent needed to make 14 per cent?

Answer by simple calculation: 1 ounce of 5 per cent and 9 ounces of 15 per cent.

(B) How much 5 per cent and 16 per cent needed to make 14 per cent?

Answered by simple calculation: 2 ounces of 5 per cent and 9 ounces of 16 per cent.

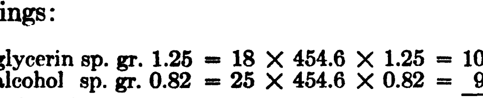
(C) How much 5 per cent and 18 per cent needed to make 14 per cent?

Answered by simple calculation: 4 ounces of 5 per cent and 9 ounces of 18 per cent.

We, therefore, have three separate batches of 14 per cent opium, all made from 5 per cent, but with higher percentage differing in every case. If we took these three separate mixings and thoroughly blended same, we would, of necessity, have 14 per cent opium, and this 14 per cent opium would originally have been made up of 1 ounce 5 per cent + 9 ounces 15 per cent; 2 ounces 5 per cent + 9 ounces 16 per cent; 4 ounces 5 per cent + 9 ounces 18 per cent; in all, 7 ounces 5 per cent, 9 ounces 15 per cent, 9 ounces 16 per cent, and 9 ounces 18 per cent, which we notice is the answer to the example as originally given.

The same method of calculation for alligation can be applied to specific gravity examples, such as: How much glycerin, specific gravity 1.25, and alcohol, specific gravity, 0.820, must be mixed to make a liquid of specific gravity 1.000? which is solved as follows:

$$\frac{1.00}{1.25 \qquad\qquad 0.82}$$ or, preferably,



Answer: 18 ounces glycerin
and 25 ounces alcohol
make 43 ounces of liquid, sp. gr. 1.00.

This example and also the percentage examples can be proved by the following reasonings:

18 fluidounces glycerin sp. gr. 1.25 = 18 × 454.6 × 1.25 = 10228.5 grains.
25 fluidounces alcohol sp. gr. 0.82 = 25 × 454.6 × 0.82 = 9319.3 grains.
43 fluidounces of liquid weigh 19547.8 grains.
43 fluidounces of water weigh 43 × 454.6 = 19547.8 grains.

Hence the mixture has about the same specific gravity as water, since 43 fluidounces of it weigh the same as 43 fluidounces of water.

The same method is used to solve such examples as:

What will be the specific gravity of a mixture of 5 fluidounces of solution of tersulfate of iron, specific gravity 1.555, and 3 fluidounces of water? The figuring being as follows:

5 fluidounces of sol. tersulf. iron = 5 × 454.6 × 1.555 = 3534.5 grains.
3 fluidounces of water = 3 × 454.6 × 1.000 = 1363.8 grains.
8 fluidounces of liquid weigh 4898.3 grains.
8 fluidounces of water weigh 8 × 454.6 = 3636.8.

Hence the liquid weighs $^{4898.3}/_{3636.8}$ as much as water and has the specific gravity 1.346.

While speaking of such examples, reference should be made to the simple example involving percentage solutions, such as: How much cocaine is needed for 1 fluidounce of a 5 per cent solution?

The absolutely accurate way of solving this is as follows:

$$\left.\begin{matrix}\text{Weight fluidounce water}\\ \text{454.6 grains}\end{matrix}\right\} \times 0.05 = 22.73 \text{ grains},$$

which represents the number of grains cocaine (hydrochloride presumably) needed to make the solution.

In this case, however, in order to obtain accurate results, the 22.73 grains cocaine hydrochloride must be weighed out, dissolved in water, and finished by bringing the finished solution up to 454.6 grains by weight, which, of course, will measure slightly less than 1 fluidounce.

Another and less accurate method, very largely employed, is by taking 5 per cent of 480 minims, or 24 grains, dissolving this in water to make a fluidounce. This, while by no means so accurate as the former process, is more convenient, and has been employed in preparing solutions of strengths under 5 per cent.

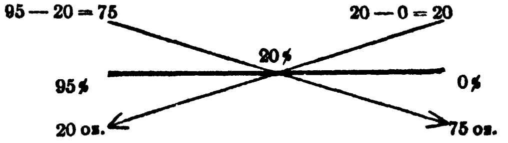
The question of what constitutes a properly prepared percentage solution has at last been settled officially by the inclusion of official directions for calculating quantities of ingredients in the U.S.P. XI (p. 4). See page 144 of this book for further comment.

A simple modification of alligation is that of percentages outlined in the U.S.P. IX under alcohol, where a rule of dilution is given. The rule is practically as follows:

If we have a 95 per cent alcohol and want to dilute it to 20 per cent, we must then take 20 fluidounces of the 95 per cent and add enough water to make 95 fluidounces; when we will have approximately 20 per cent alcohol.

It may also be solved by the regular process of alligation if we recast the problem to the following wording: How much 95 per cent alcohol and 0 per cent alcohol (water) needed to make 20 per cent alcohol?

Solved by "rule of the balance,"



This shows that we can reduce 95 per cent alcohol to 20 per cent by reversing the fluidounces with the percentages. That is, from 20 fluidounces of 95 per cent alcohol we can make 95 fluidounces of 20 per cent. But suppose the questions is: How much 20 per cent alcohol could be made from 5 fluidounces 95 per cent? It is a case of simple proportion.

If 20 fluidounces 95 per cent give 95 fluidounces 20 per cent, 5 fluidounces 95 per cent (¼ of 20) will give us ¼ of 95 fluidounces 20 per cent, or 23¾ fluidounces.

Expressed in proportion:

$$20 : 5 : : 95 : x$$

$$x = \frac{5 \times 95}{20} = 23\tfrac{3}{4} \text{ fluidounces.}$$

It is important that this be understood. The rule, by the way, applies *exactly* only when there is no diminution in volume.

BIBLIOGRAPHY

Hydrometers.—(History) Dornke and Reimerdes, Handbuch der Aräometrie, 1912; Bourgougnon, Ch. Zt. Rep., 16, 1892, 166; Lippmann, Ch. Zt., 36, 1912, 385 and 629, and 39, 1915, 985. (General) Schelenz, Ch. Zt., 27, 1903, 88 and 39, 1915, 913; Schroeder, Chem. App., through C.A., 8, 1914, 3385. (Baumé's) Pilé, A.Ph.A., 18, 1870, 155; Pemberton, A.J.P., 24, 1852, 1; Anon, Bur. Standards Circ., 16 (1914) 1–16, and 59, 1916, 1–13; Taber, Jl. Ind. Eng. Ch., 12 (1920) 593; Schelenz, Zt. angew. Ch., 33, I (1920) 208; Horne, Jl. A.O.A.C., 4 (1921) 551; Wallis, Chem. Fab., through Jl. Soc. Ch. Ind., 48, 1929, 343B.

Mohr-Westphal Balance.—Anon, N. R., 6, 1877, 78.

Density of Wax.—Hager, Analyst, 4, 1879, 206, Dietrich, Pe.Zt., 32, 1887, 37.

Density of Heavy Solids.—Vuilleumier, Jl. Ind. Eng. Chem., 16, 1924, 620.

CHAPTER IV

HEAT AND REFRIGERATION

HEAT is that form of molecular motion which produces the physiologic sensation we call warmth, this molecular motion being produced by friction, electricity, light, or chemical action. In order to obtain a clear understanding of heat, a comprehension of the molecule as explained on p. 384 is essential. Suffice it to say here that molecules are very minute particles of matter, and these molecules, working among themselves, produce friction. That *friction* is the source of heat is well known, and can be demonstrated by such simple experiments as rubbing one surface on another when both become hot. This is shown by rubbing the finger rapidly on a piece of wood, when the sensation of warmth is transmitted to the body. It is also known that when any metallic body, such as an axle, rubs rapidly on its bearings, if the axle is not well greased to prevent this friction, the heat produced is sufficient to set fire to the surrounding objects, producing the condition called "hot box." Primitive people, such as Indians, becoming adept at the art, were able to kindle fires by rubbing two pieces of wood together.

In each case we have a striking illustration of friction as a source of heat.

Another source of heat is *electricity*, and in such cases the friction of the molecules of the nonconductor produces heat. In many cases the resistance causes the substance to glow or become incandescent. Such is the basis of the incandescent electric light in which the electricity is forced through a filament of carbon or of some poorly conducting metal, the molecules in the filament in resisting the electric pressure are heated sufficiently to become incandescent.

A discussion of the principles of electricity is beyond the scope of this work, and for details of this force the reader is referred to any standard textbook of physics.

Suffice it here to state that electricity is a molecular condition, and that this condition is transmitted from one molecule to another with more or less rapidity, dependent on the character of the substance influenced. Matter which rapidly transmits the electric condition from one molecule to another is called a conductor of electricity, while matter the molecules of which do not transmit the condition is said to be a nonconductor or a poor conductor.

As the question of conduction of electricity is a purely relative matter—all bodies transmitting the condition to an extent more or less great—the terms above mentioned are gradually becoming obsolete, and the words "conductivity" and "resistance" being substituted to cover the respective meanings. When we talk of "the electric current" passing through a wire, we mean that the electric condition affecting the end molecule of the wire is rapidly transmitted to the adjoining molecule, and thence from one molecule to another, the whole length of the wire. This being clearly understood, we can use the simpler term, "passage of the electric current," in the following explanations.

Electricity passes rapidly from molecule to molecule through a conductor; but if compelled to run through a nonconducting substance, it requires a current of high potential, of great force, to overcome the resistance of this body.

Light also affords a minute amount of heat. Heat, light, and electricity are so-called "physical forces" affecting molecules, and are, under certain circumstances, convertible one into another.

We have just seen that electricity is converted into heat; inversely, heat can be converted into electricity.

By applying heat to two metal plates in close contact with each other, an electric current is formed in the apparatus known as the "pyro-electric battery." Hence it is not strange that light can be converted into heat, although the amount produced is very minute and very difficult to measure, inasmuch as almost invariably all sources of light are also sources of heat, and, therefore, it is very difficult to isolate light from its accompanying heat.

Chemical action is the chief source of heat. This phenomenon, which is fully described on p. 384 means a breaking up of the molecules of a substance, with the formation of new molecules. This decomposition is accompanied with considerable movement of the molecules and their constituent atoms, thus producing a form of friction and, therefore, producing heat.

Combustion.—Most chemicals reacting on one another produce heat, although in some cases the reverse is true. As an illustration of heat produced by chemical action, iron combined with iodine in a test tube in the presence of water will so heat the test tube as to render it difficult to hold same in the hand. Likewise, sulfuric acid combined with solution of soda produces great heat, and numberless other illustrations could be given. The production of heat by such chemical action is different from the chemical action in the burning of wood. The invariable accompaniment of the latter being flame, such form of chemical action is called *combustion,* that is, chemical action accompanied by heat and *light.* We know that wood is composed of hydrogen, oxygen, and carbon; that the air around us contains oxygen, and that by applying a flame to the wood there is commenced a chemical reaction which results in the formation, from the carbon, hydrogen and oxygen that is present, of carbon dioxide (CO_2) and of water (H_2O).

In this chemical reaction, as in the formation of ferrous iodide, heat is produced, and of much greater intensity. So great is the heat that some of the carbon, which in the hurry of the reaction escapes combination with the oxygen; glows with heat, just as does the tungsten filament in the incandescent lamp. To prove the presence of incandescent carbon hold a plate over any luminous flame, when it will become blackened with soot, which is pure carbon. Whenever the combustion—as we call reaction, in which the carbon and hydrogen of a substance combine with the oxygen of the air—is accompanied by unchanged carbon glowing with heat, a flame is produced.

Any substance with which we can perform a combustion is called fuel. Such matter is very abundant, and is found in all three states of aggregation—solids, liquids, and gases.

Solid Fuels.—The solid fuels are wood, coal, coke, and charcoal. Wood contains hydrogen and oxygen besides carbon, whereas coal, coke, and charcoal consist largely of carbon. In the case of each fuel the chemical action involved is the combination of the carbon with the oxygen of the air, forming carbon monoxide and carbon dioxide, with more or less particles of unconsumed carbon, called soot.

In burning solid fuels the apparatus designed to contain same is called stove or furnace, and consists fundamentally of the fire-box in which the fuel is held, the chimney or flues for removal of the gaseous products of combustion, and damper or vents for the admission of air necessary to produce the action. Provision is made, by means of grating, for the removal and storage of ashes, which constitute the inorganic salts present in wood or coal.

In order to produce successful combustion the oxygen of the air is absolutely necessary, hence if a furnace or stove is not supplied with sufficient air, the fire within the box will be "smothered" or "go out." This explains the method of smothering a fire by surrounding the burning substance with blankets, thus preventing access of air. In order to produce good combustion, a comparatively good draft of air must be had, the intensity of the draft being regulated by the opening or closing of the vents or dampers, and in large furnaces by the relative height of the chimney or smoke stack.

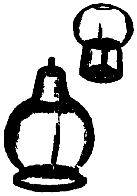


Fig. 37.—Spirit lamp.

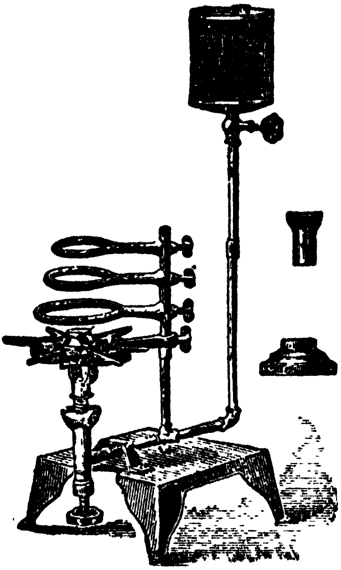


Fig. 38.—Vapor stove and burner.

For the practical application of combustion of solid fuels the reader is referred to any kitchen range or house furnace.

The liquids used as fuels are alcohol and petroleum products (gasoline and insurance oil, etc., and, latterly, crude petroleum). In using liquids as fuel there are three methods employed:

If the liquid is not very volatile, such as insurance oil, astral oil, etc., the liquid is sucked up through a wick by capillary attraction, and burned as a liquid off the top of the wick. Such a method is also employed in the burning of the volatile liquid alcohol in the ordinary alcohol lamp (Fig. 37).

In cases where the liquid is quite volatile (as gasoline), the apparatus used for the purpose is so arranged that the liquid is first converted into vapor and this vapor burned. Such is the principle of the vapor stove (Fig. 38), which possesses a great advantage over the wick stoves by having the vapor burned mixed with air, as in the Bunsen burner, thus preventing a sooty flame. Alcohol is also burned in the form of vapor in the so-called "Russian blast lamp," which produces an intensely hot flame (Fig. 39).

Where oil such as crude petroleum is used as a fuel it is necessary, in most oil heaters, to atomize it, that is, split it up into a fine spray and for this purpose three methods may be adopted, namely, atomizing by means of steam, compressed air, and pressure. There is usually a mixing chamber in which oil and air are mixed before combustion in the furnace. Where atomizing is not resorted to, oil is converted to gas by means of a preheating device, mixed with air and blown into the combustion chamber by means of a fan.

Liquid Coal.—By means of the Bergius process powdered coal is liquefied by heating with hydrogen under pressure. The introduction of 5 per cent of hydrated ferric oxide assists the process by combining with sulfur contained in the coal and also possibly acts as a catalyst. A large amount of heat is produced by the hydrogenation process.

Gaseous Fuels.—The gases used to produce heat in pharmacy are coal-gas, acetylene, and natural gas, the first two being manufactured, while the latter is obtained in certain sections of the world by simply sinking iron tubes, through which the gas escapes from pockets under the earth's surface.

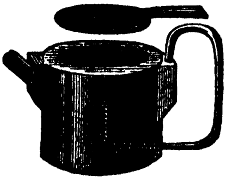


Fig. 39.—Russian alcohol blast lamp.

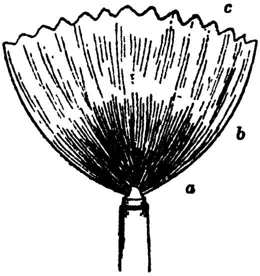


Fig. 40.—Fish-tail flame.

As to the manufacture of artificial gas, coal-gas is made by the destructive distillation of coal; details of the manufacture can be found in any advanced work on technical chemistry. Acetylene is produced by the action of water on calcium carbide.

Chemically, these fuel gases resemble one another, all being combinations of carbon, which furnishes the heat and light when consumed in the presence of air in the operation of combustion in different forms of burners, according as the intention is to produce a luminous or a nonluminous flame, the latter being used for heating purposes.

A luminous flame is produced in the so-called "fish-tail" burner, in which the gas, as it comes in contact with the air, is ignited by a match or other flame, burning to carbon dioxide and water with incomplete combustion; that is, in the reaction all the carbon is not consumed, and the unconsumed carbon, through the influence of the intense heat generated by the chemical reaction, glows with heat, or, technically expressed, becomes "incandescent." Another example of incandescence is the brilliant light produced when metallic magnesium is burned (p. 514).

Why can some part of the carbon escape chemical combustion?

Bear in mind that the combination is with the oxygen of the air; that the gas evolving from a fish-tail burner forms a mass of some thickness.

The oxygen of the air can combine only with the outer surface of this mass, leaving the inside of the flame untouched; just as a tightly closed book, when immersed in water, will be soaking wet on the outside and comparatively dry inside. That gas inside the flame has not enough oxygen to convert all the carbon into carbonic oxide, and the result is that much of the carbon remains unchanged, glowing with the heat of the ardent reaction, and depositing as soot when it passes from the flame. The fish-tail flame (Fig. 40) may be quaintly likened to a chemical factory. Zone *a* is the reception room, where the crude material that is to be worked up—the gas from the mains—comes in; zone *b* is the workshop where the chemical reaction is carried on with the utmost vigor—where the hydrocarbon of which the gas is composed is broken into carbon and hydrogen, and these in turn combine with the oxygen of the air to form carbon dioxide and water; while zone *c* is the shipping-room, whence the finished products just mentioned are sent away. Since the soot is dirty and inconvenient in cooking, efforts were made to so construct a burner that the gas would have contact with the air (or its oxygen, for air is composed of nitrogen, oxygen, and some carbon dioxide), in parts other than the outer surface, and this is done by mixing the gas with air before burning it in the Bunsen burner. Aside from the great advantage of freedom from soot, the flame of the Bunsen burner is superior to the ordinary flame by reason of its greater heat. In it all the carbon of the gas becomes combined with the oxygen of the air, and it is self-evident the more chemical reaction occurs in a certain space (as in the mass of gas issuing from a burner), the greater will be the heat produced.

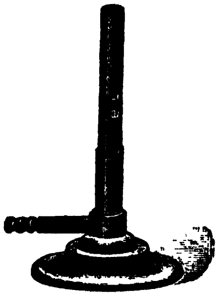


Fig. 41.—Bunsen burner.

With this purpose in view the Bunsen burner is constructed with a few modifications, according to the purpose adapted. In its simplest form it consists of an upright metallic tube with orifices at the bottom, and as the gas rushes upward through the tube, it mixes with air that enters through the bottom orifices, and when emerging from the top of the tube and ignited, it contains sufficient air thoroughly to combine with all the carbon, thus producing carbon dioxide and water, and no unconsumed carbon or soot. Such a burner (shown in Fig. 41) gives a flame in which three zones can be noted on close scrutiny (see Fig. 42). The top of zone "*a*" is called the reducing flame, while the top of zone "*b*" is the oxidizing flame (Fig. 40).

This long accepted view of the gas flame has been submitted to criticism. Smithells states that in zone "*a*" all of the carbon has been changed to carbon monoxide, and that the changing of the flame from a luminous to a nonluminous one can be accomplished as well with carbon dioxide, steam or even nitrogen. Armstrong inclines to the belief that combustion is due to the reactions between the fuel, oxygen, water, and certain catalysts found in the fuel; in short, the reactions are far more complex than the classic statement:

$$CH_4 + 2O_2 = CO_2 + 2H_2O$$

In using such a Bunsen burner the flame sometimes "strikes back," that is, the gas which is ignited at the top of the tube finally catches fire at the bottom of the tube, where the unmixed gas emerges, thus producing a sooty flame, and at the same time heating the brass tube, sometimes to a dangerous extent. Such a striking back can be avoided only by having a good current of gas turned on. It can usually be detected from a distance by the peculiar odor of acetylene generated in this incomplete combustion.

The Méker, Teclu, and Scimatco burners are improved forms of the Bunsen burner in which according to the inventors, a maximum quantity of gas is produced in a minimum volume of flame; the result is a very hot flame of uniform temperature throughout (Figs. 42 and 43).

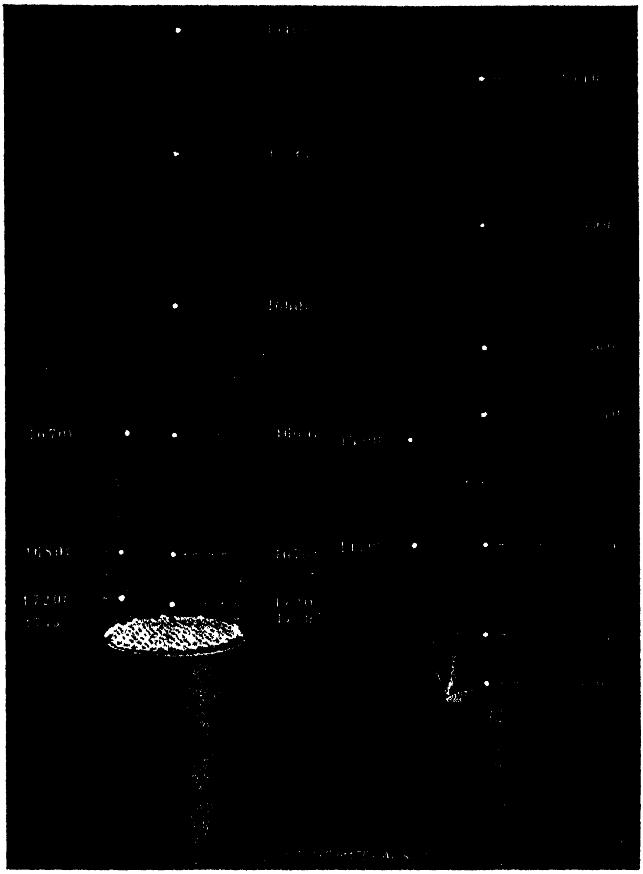


Fig. 42.—Flames of Méker and Bunsen burners.

For the purpose of more extended heating, larger varieties of the so-called "gas stove" are obtainable, the most practical of which, from the pharmacist's standpoint, being the Fletcher radial burner shown in Fig. 44, in which the gas is mixed with the air in a horizontal tube, and emerges through radiating slits cut into a central dome, thus making a flat, clean, and intensely hot flame.

Internal Combustion.—Brunler and others have shown that under proper precautions a nonluminous oil or gas flame inverted and immersed into a vessel containing water, will actually continue to burn. Brunler has put upon the market internal combustion boilers based upon this principle.

Surface Combustion.—Mixtures of gas and air in proper proportions brought into contact with heated porous material will burn with intense heat without giving much flame. Ovens of this kind are now being constructed.

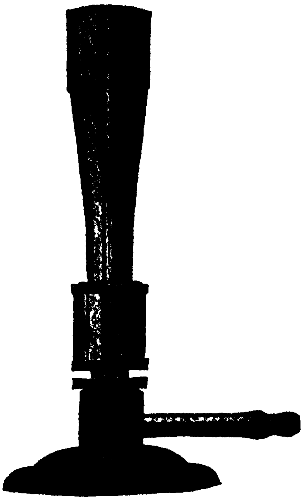


Fig. 43.—The Scimatco burner.

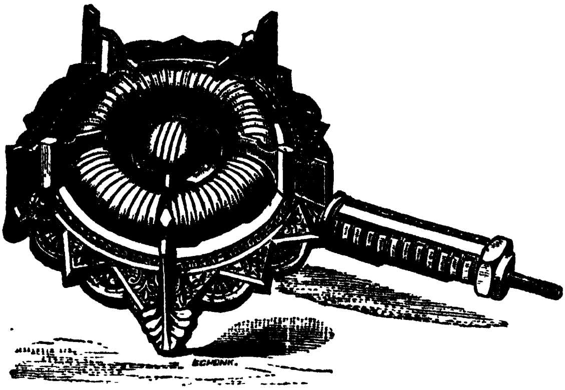


Fig. 44.—Fletcher's radial burner.

BLOWPIPES

The principle of the blowpipe is merely an extension of the principle of the Bunsen burner. With the blowpipe, the air expelled from the lungs is blown through the tube upon the flame, thus insuring a complete combustion of the gas. The blowpipe produces more heat than the Bunsen burner, for the reason that in blowing air into the flame the flame is rendered much sharper and narrower than in a Bunsen burner, and in this way heat produced by chemical action is concentrated to a more limited area; hence by this instrument we are able to make a very intense heat, albeit in a very narrow area.

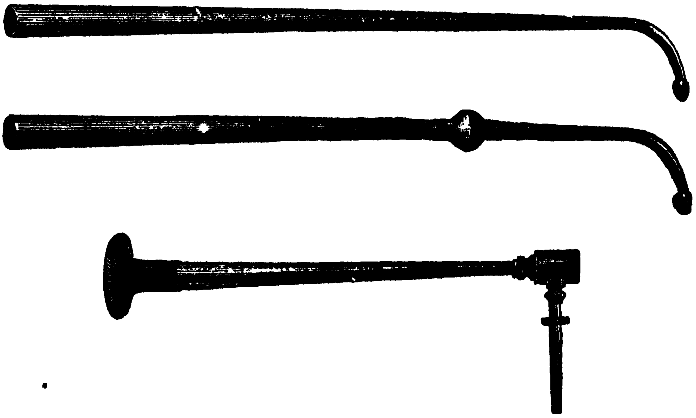


Fig. 45.—Blowpipes.

The blowpipe consists of a bent and tapering brass tube ending in a very minute orifice, the larger end connecting with an appropriate mouth piece which is pressed firmly against the lips when the air is energetically blown from the lungs through the pipe into the flame. In the cheaper forms of such blowpipe, where no mouth piece is provided, the larger end should be fitted with a piece of rubber tubing to prevent the lips coming in contact with the brass, which causes irritation. The continuous blowing of air through the blowpipe is merely a matter of practice, the expert being able to inhale through his nose at the same time that he forces the air from his lungs through his mouth into the blowpipe, and this must be done if a continuous flame is desired (Fig. 45).

The blowpipe is used entirely for minute operations, such as small chemical work, or for insignificant cases of soldering in the jewelry business. For large operations in which a concentrated flame of high intensity is desired the *blast lamp* (Fig. 46) is used, and this is merely a modification of the blowpipe in that the air is furnished by means of the bellows or compressed air rather than by the lungs, and thus the instrument can be made larger.

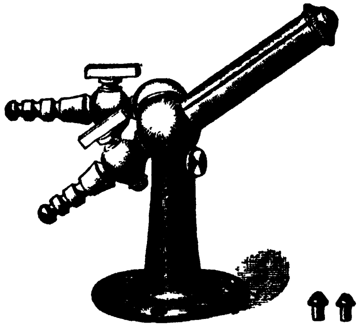


Fig. 46.—Blast lamp.

In such a blast lamp a rather large flame of great intensity (1700° C.) can be easily attained, with the sole physical outlay of operating the bellows with the foot or where a system of air compression is available, as in most well-equipped laboratories, by merely turning on and regulating the air intake. When a very intense flame is desired, the same blast can be applied, but instead of illuminating gas, hydrogen is pumped in, and instead of air, oxygen is supplied. This forms the oxyhydrogen blast lamp, and with this instrument a heat sufficient to melt platinum (about 2000° C.) can be attained. Acetylene and oxygen mixtures are likewise employed to furnish intense heat through the oxyacetylene torch which is used extensively in welding and cutting steel and metals.

Electricity is also used for the production of heat, and in future will play a more important rôle in our domestic economy. Electric stoves are used increasingly for cooking purposes, while the greatest artificial heat is derived by the use of the Moissan electric furnace.

An interesting method of production of heat without flame is shown in the use of *thermite.* (See p. 545.)

The following table of relative temperatures of the commonly used heating appliances may be of interest.

Bunsen burner (Fig. 42):	
Lower part of zone "*a*"	300° to 500° C.
Zone "*b*"	1540° to 1560° C.
Méker burner	1650° to 1780° C.
Natural gas	1800° to 2000° C.
Methane	1875° C.
Propane	1930° C.
Carbon monoxide	1960° C.
Coal combustion (maximum)	2000° C.
Electric arc (common electric furnace)	2000° to 3500° C.
Atomic hydrogen	2490° to 2540° C.
Oxyacetylene flame	2500° to 3400° C.
Oxyhydrogen blowpipe	3200° C.
Moissan electric furnace	4000° C.

BATHS AND OTHER REGULATING DEVICES

Baths in pharmacy are devised for uniform distribution or for the limitation of heat. Thus the heat of a Bunsen burner, while very satis-

factory, is apt to be more intense on one portion of the utensil being heated than on another, and to this cause is due most of the fractures on heating glass and porcelain utensils.

It is a dictum that, in heating substances in porcelain or ordinary glass utensils, the direct heat of a Bunsen burner should never be applied, but the flame should be uniformly distributed in the several ways at our disposal. The simplest form for the uniform distribution of heat is a sheet of asbestos or of tin, by which the cylindric flame of the Bunsen burner is spread out to the entire surface of the interposing medium, and a uniform heat is in turn transmitted from it to the container above.

Wire Gauze.—Far more convenient than these, however, is a piece of gauze made of iron, copper or "nichrom" wire. Through such gauze the heat more readily penetrates than through asbestos, and at the same time the heat is as uniformly distributed by reason of the fact that the wire of which the gauze is constructed is an admirable conductor of heat, and the moment the flame comes in contact with the gauze, each of its many filaments aid in drawing the heat to every portion of the gauze. This has the effect of chilling the flame itself, hence such flame cannot pass through a wire gauze until the gauze has become heated to a temperature almost equal to the flame.

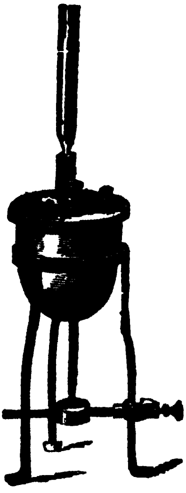


Fig. 47.—Meyer's toluene bath.

On this principle is based the construction of the Davy safety lamp for use in mines, the use of which is of no pharmaceutic importance.

This phenomenon also explains why smoke cannot penetrate through such gauze, hence the value of gauze in the old form of gas stove.

Sand Baths.—A sand bath consists of a suitable flat dish in which is put a sufficient quantity of sand, the container of the liquid to be evaporated is placed therein, and the sand is piled around so as to completely surround it. Heat by means of the Bunsen burner or other flame is applied under the dish, and is uniformly transmitted to all portions of the heating substance by way of the heated sand.

In this form of bath the heat is limited only to the amount produced by the burner, the sole aim being to distribute the heat uniformly.

Liquid Baths.—These consist of a suitable dish containing the liquid which is to be heated, the heat of which is in turn transmitted to the substance which it is desired to make hot.

The liquids used for this purpose are oil, glycerin, salt water, and water.

The *oil bath*, like the sand bath, uniformly transmits heat, but in addition thereto limits the amount of heat by reason of the fact that when the temperature of 260° C. is attained, the oil begins to burn; that is, undergoes decomposition, with the formation of the stifling vapors of acrolein, which serve as a warning to the operator that a high heat has been attained.

Glycerin baths act on the same principle of operation as the oil bath, and are limited for the same reason to 250° C. Both forms of baths are, not so much used now, by reason of the fact that they do not really limit heat, and their method of warning to the operator is too disagreeable to be popular. In their place, liquid petrolatum is used as the heated fluid.

Toluene and *xylene baths* are sometimes used (see Fig. 47).

These liquids, boiling at 110° C. and 140° C. respectively, are placed in a jacketed vessel provided with a long glass tube, which acts as an upright condenser, causing the vapors to chill to a liquid and drop back into the container. In applying heat to such a bath the temperature rises to the boiling point of the liquid, and the vapors, being condensed and returned to the container, are not lost; hence in such a bath we have not only the limit of temperature, but it also offers a practically perpetual operation.

A *salt-water bath* is based on the same principle as the water bath, save that it consists of an aqueous solution of some salt whereby the temperature of the boiling liquid is raised.

A bath made of salt water—saturated solution of sodium chloride—was formerly considerably used under the Latin name, "balneum maris." Such a bath, however, possesses the great disadvantage of losing water by evaporation, with solidification of the remaining saline solution. It is, therefore, comparatively little used.

A saturated solution of sodium chloride boils at 108.6° C.; of potassium chloride at 108.5° C., of sodium sulfate at 102.8° C.; of potassium sulfate at 101.3° C.

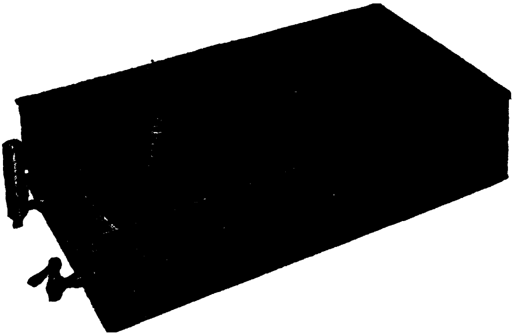


Fig. 48.—Precision monel metal water bath. (Courtesy Precision Scientific Company.)

Since 1917, baths containing melted crystalline chemicals have been employed for certain purposes. Thus Sollmann utilized crystalline sodium acetate (m.p. 68.5° C.) for keeping paraffin dressing (p. 361) melted; while Benesch recommends crude sodium bisulfate (m.p. 145° C.) for the same purpose.

Water Baths.—In these the liquid to be used is water, and since water boils at 100° C., the temperature of the bath never rises above that point. A consideration of why water does not boil over 100° C. is left for a subsequent page, and, therefore, attention need be paid only to the various forms of water bath (Fig. 49).

There is comparatively little necessity for buying expensive apparatus for use as a water bath. Any tin pail filled with water in which the evaporating dish can be rested, or into which the flask can be sunk, can be used. An excellent form of expensive water bath is a continuous steam apparatus shown in appended cut (Fig. 50). In this the water trickles from faucet into the well, *a*, the excess passing into the drain by overflow pipe *b*. A lighted Bunsen burner is placed beneath the well, and the amount of water is rapidly converted into steam. An elaboration of this type of water bath made of monel metal (p. 594) and heated by steam is now available (Fig. 48).

Steam Bath.—The steam bath differs from the water bath inasmuch as the substance to be heated comes in contact with steam rather than with boiling water. While steam possesses the same temperature as boiling water (100° C.), it has a much larger actual quantity of heat, as will be explained under the subject of Latent Heat (p. 102).

Suffice it, therefore, to say that while in the steam bath, where the steam is brought into contact with the object to be heated at the ordinary atmospheric pressure, it will transmit to the same a temperature of 100° C.; on the other hand, if the apparatus is so arranged as to bring steam under pressure into the bath, a higher degree of heat can be attained. Thus, under the normal atmospheric pressure, 14.7 pounds to the square inch, steam has a temperature of 100° C., while if steam is forced in until the pressure of 100 pounds to the square inch is obtained, said steam will have a temperature of 164° C. Steam of any pressure above that of the normal atmosphere is said to be superheated. In large manufacturing concerns, steam, either under normal pressure or in the superheated state, is used in most of the evaporation processes.

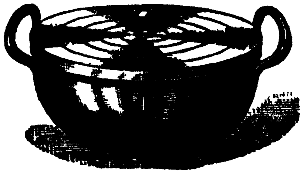


Fig. 49.—Copper water bath.

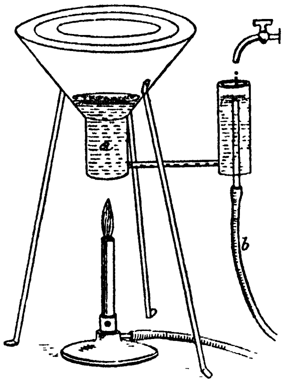


Fig. 50.—Meyer's water bath.

As steam baths are rarely used in retail pharmacy, a further consideration of the subject is omitted, the reader being referred to some textbook on advanced physics for information concerning laboratory steam kettles used for open pressure, and steam coils in which the steam can be heated under normal pressure or in superheated condition. A well-known variety of steam coil is the steam radiator, so largely used in heating houses.

The advantage a steam coil possesses from the manufacturing standpoint is that it can be placed directly into the kettle containing the substance to be cooked, and thus the substance can be directly heated, with practically no loss by radiation.

REFRIGERATION

Refrigeration is the removal of heat by use of certain mechanical devices. Beginning several centuries ago, by use of "ice-boxes," modern refrigeration may be said to have started when Carré (1867) and Linde (1874) designed ice-making machines based upon the cyclic evaporation and compression of such gases as ammonia, carbon dioxide, and sulfurous oxide. Artificial ice factories were established in the United States during 1875 to 1880 and ice manufacture has become a great industry. Later developments of refrigeration were the erection of cold-storage warehouses, of small refrigerating units on ships and, latterly, in household refrigerators. Cooling houses and trains by "air conditioning" is now being accomplished.

The gases used in these several refrigeration units include ammonia, carbon dioxide, sulfur dioxide, dichloromethane (or *carrene*), dichloroethylene (or *dieline*) dichlorodifluoromethane (or *freone*), and methyl chloride. Carbon dioxide in solid form is now commercially available under the name of *dry ice.*

It is unnecessary to dilate upon the need of a refrigerator in every pharmacy. As Hallberg put it years ago, the average retail druggist is willing to put $1000 or $2000 into a refrigerator for soda water and begrudges $100 for an ice-box. Modern medicine demands that biologicals be stored in a refrigerator. Such unstable pharmaceuticals as syrups and ointments should likewise be kept in cold storage.

EVALUATION OF HEAT

While we commonly speak of a thermometer as an instrument used to measure heat and cold, this definition is only partly true, as by means of the thermometer we measure the intensity of the heat, but not the actual quantity produced. Thus, while it is true that with a flame producing a temperature of 500° C. we can accomplish more heating in a given time than we can with a flame of 150° C., nevertheless, if we use a flame of 150° C. for a sufficient length of time, we can usually accomplish as much as with a 500° C. flame for a shorter time, although there are, of course, certain operations in which the intensity of heat is essential and a lower intensity would not do, even though applied for a proportionally longer time.

For measuring the actual quantity of heat—the amount of work done by a flame—the unit called the calorie has been devised.

A calorie represents the amount of heat necessary to raise 1 Gm. of water from zero to 1° C., and will be spoken of more fully in the discussion of latent heat. There is also the so-called "large calorie" which equals 1000 "small calories."

THERMOMETERS

Thermometers are instruments used for directly measuring the intensity of heat, but only indirectly the quantity thereof. Most of these instruments are based on the expansive power of certain liquids and gases. It is characteristic of a large number of varieties of matter to expand with a rise in temperature and, indeed, in regular proportion to the increase in temperature. Thus, an iron bar when heated expands, and if the expansion is limited to the longitudinal direction by encasing the bar in some way so as to prevent excessive lateral expansion, the expanded bar can be made to operate on a lever which moves a needle on a dial, and thus represents the intensity of heat, or the temperature. Such is the simplest form of the so-called "*pyrometer*," which is intended to indicate temperatures greater than those shown by the ordinary form of thermometer.

To obtain an accurate thermometer the expanding substance should be liquid or gaseous, and in the early days such forms were devised, the first being by Galileo, who devised an air thermometer, in which the expansion of the air in a flask operated on a tube containing water. As the air expanded or contracted, the column of water fell or rose in the tube and in this way changes in temperature were crudely estimated.

Similar rough instruments were devised from time to time, but the first step in the scientific direction was made by Fahrenheit between 1709 and 1724. Fahrenheit's first improvement was to use mercury in the thermometer instead of water or alcohol. The expansion of mercury is very delicate, and the density of this liquid being so much more than water, it would require a great deal less of it than of water or alcohol; hence in the Fahrenheit thermometer a much smaller tube was necessary than in the alcohol thermometer.

It is claimed that Ismail Boullian made the first mercury thermometer in 1659, but this was not used at the time that Fahrenheit devised his thermometer.

Fahrenheit also devised the first acceptable system of graduation, and this method, somewhat modified, is in use to this day. In graduating this thermometer Fahrenheit set about to find absolute zero, and finally decided that the greatest cold possible was that produced by a mixture of ice and salt. He prepared such a mixture, plunged his thermometer into it, and marked off the place where the mercury stood at this temperature, and denominated this point zero.

That the temperature of ice and salt is the greatest cold produced has proved false. It is usual, every winter, to find certain sections of the world where the temperature falls to as low as 50° or 60° below zero, while experiments of physicists indicate that absolute zero is $-273°$ C.

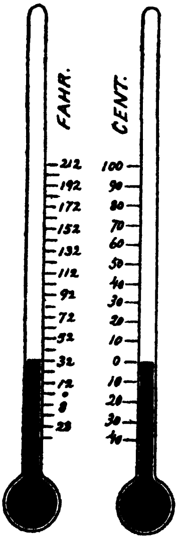


Fig. 51.—Comparison of Fahrenheit and centigrade thermometers.

Fahrenheit, however, having arranged his zero to his own satisfaction, next turned to look for another authoritative standard, and for this he determined upon the temperature of the blood. He, therefore, placed his thermometer under his arm, noted the point to which the mercury rose, marked the space, and, for some reason not explained, denominated this "24." The space on the tube between zero and 24 he divided into 24 spaces called degrees, and his later experiments showed that on such a thermometer melting ice registered 8 degrees.

Such a thermometer was intended for practical use, but it was soon found that the range of 24 between his zero and the temperature of the blood was scarcely sufficient for practical purposes, hence he devised a thermometer in which his former degrees were multiplied by four, and on such thermometer the melting point of ice was 32 degrees, and the temperature of the blood 96 degrees, and in terms of these degrees the boiling point of water registered 212 degrees.

Fahrenheit's thermometer, while a step in the right direction, has the misfortune of being based on an unscientific standard, as ice and salt do not produce the lowest known temperature, and, moreover, do not always represent exactly the same temperature as experience has long since proved. In the same way the statement that 96 degrees is the temperature of the blood is not absolutely accurate, inasmuch as the blood's temperature varies according to the condition of the person.

The graduation adopted by Réaumur in 1730 was a decided advance over the Fahrenheit system, inasmuch as Réaumur took for zero an absolute standard very easily determined (the melting point of ice), and chose for his higher standard the equally accurate and easy unit of the temperature of boiling water. The latter, however, he denominated 80 degrees, and the scale was, therefore, much improved by Celsius in 1740 in devising his centigrade system, in which the melting point of ice is zero and the boiling point of water 100 degrees, and the space between was accurately divided into 100 parts.

A comparison of the thermometers can be best shown by appended sketch (Fig. 51), in which it can be noted that while in the Fahrenheit thermometer the space between the freezing point and boiling point is divided into 180 degrees (212 to 32 degrees), the same space on the Celsius is divided into 100 degrees. Therefore, we can sum up the relative values as follows:

180° F. = 100° C.
1.8° F. = 1° C.

To sum up:

Fahrenheit....	Melting point, 32°	Boiling point, 212°	Difference, 180°
Centigrade...	" " 0°	" " 100°	" 100°

which evolves the very important point that *1° centigrade equals 1.8° Fahrenheit.*

If both Fahrenheit and centigrade had the same zero, or starting point, the conversion of one into the other would be very simple, as it would only mean multiplying or dividing by 1.8, but where zero appears on Celsius (or centigrade) scale, the Fahrenheit equivalent is 32 degrees and this 32, accordingly, comes in as a factor in changing one kind of degree into the other.

The rules of conversion can be abbreviated thus:

C. into F.: × 1.8 and +32; F. into C.: −32 and ÷ 1.8, to which might be added for temperatures *below the freezing point of water* that the addition and subtraction are by the rules of algebra.

To explain this, sketch a thermometer, similar to that pictured above, with centigrade markings on one side and Fahrenheit on the other, beginning with a line marked 0 on the centigrade side and 32 on the Fahrenheit.

Suppose we have 50° C. as a starter:

50 × 1.8 = 90.0, *i. e., 90 Fahrenheit degrees* but not *degrees Fahrenheit.* It means 90 Fahrenheit degrees above the melting point of ice, and this point is 32 Fahrenheit degrees above the Fahrenheit zero. To get the actual *degrees* Fahrenheit in 50° C. we must add this 32 to the 90 already gotten, when we find that 122° F. = 50° C.

We will try the reverse problem: How many degrees Centigrade in 122° F.? We first get this figure on the same basis as zero Centigrade. This we do by subtracting 32 from 122, thus finding how many Fahrenheit degrees 122 degrees is above the melting point of ice. The difference between 32 and 122 is 90, and this, divided by 1.8, gives us 50. Therefore 122° F. equals 50° C.

Below the melting point of ice, the matter is a little more difficult. Let us choose as our example how many degrees Fahrenheit in −35° C.

35 × 1.8 = 63 Fahrenheit degrees, *not* degrees Fahrenheit, below the melting point of ice—63 Fahrenheit degrees below the point that is marked zero on the centigrade scale. The point marked zero on the centigrade scale means 32° F.; so the 63 degrees we have spoken of will be partly above and partly below zero Fahrenheit; 32 degrees of it will be above zero, the balance (63 − 32), which is 31 degrees, will be below zero Fahrenheit, and thus we see that −35° C. is equal to −31° F. Inversely, if we want to know the value of −31° F. in the centigrade scale, the first thing to do is to find how many Fahrenheit degrees there are between −31 degrees and that point on the Fahrenheit thermometer which equals 0° C. This point is 32° F. If there are 31 degrees below zero and 32 degrees above that point to 0° C., then the number of Fahrenheit degrees between −31° F. and the point marked zero on the centigrade scale is 31 + 32 = 63.

In other words, −31° F. is 63 Fahrenheit degrees below zero centigrade. Take 63, divide by 1.8, and we get 35, showing that −31° F. equals −35° C.

It would be useful for the student to calculate in centigrade degrees the value of −40° F. (see p. 610). A simple method of conversion suggested by LaWall that may appeal more forcibly to some students than the foregoing may be expressed as follows:

C. into F.: add 40 and multiply by $\frac{9}{5}$ and then subtract 40.

F. into C.: add 40 and multiply by $\frac{5}{9}$ and then subtract 40.

Conversion of Fahrenheit markings into Réaumur and Réaumur markings into Fahrenheit is of comparatively little importance in American pharmacy; therefore, a brief statement of the factor will suffice.

If 0.8° R. = 1.8° F.

Then, 1° R. = $\frac{10}{8}$ × 1.8, or 2.25° F.

Then to convert Réaumur into Fahrenheit multiply by 2.25 and add 32.

Then to convert Fahrenheit into Réaumur subtract 32 and divide by 2.25.

Varieties of Thermometers.—The usual form of thermometer consists of a glass bulb to which is attached a capillary tube. In it is placed a sufficient quantity of boiled mercury to fill the bulb and the lower portion of the tube. In the cheaper form of thermometer air is allowed to remain in the rest of the tube, which is sealed at the other end. In such thermometers, however, after continued use, the mercury is gradually oxidized by the air, rendering the instrument less accurate; therefore in the finer grades of thermometer the air is replaced by pure nitrogen, or a vacuum is made in the tube. This bulb and tube is then attached to a scale in the several ways that convenience suggests, the cheaper forms of thermometer being merely fastened to a piece of wood on which the scale is marked, while the chemical and pharmaceutic thermometers are usually inclosed in a glass tube inside of which the scale is placed, the intention in this case being to make the thermometer of cylindric form and sufficiently small to permit insertion through a cork, and then into the neck of a flask. On such thermometer the scale is made of paper or porcelain placed inside of the outer tube, or else it is engraved on the outer surface of the outer tube, the latter being particularly the case in the exceedingly small and delicate thermometers used in determining boiling and melting points (Fig. 52).

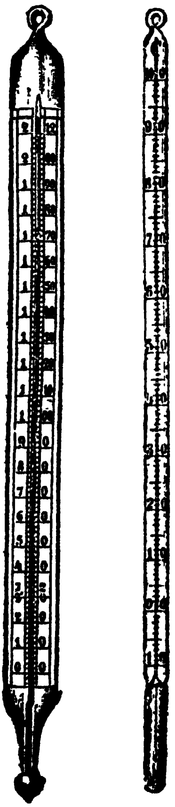


Fig. 52.—Chemical thermometers.

In purchasing a thermometer for pharmaceutic purposes, always avoid those with paper scales, for should one be heated above 125 degrees, it will scorch and even char, and the reduction in cost, as compared to the porcelain scaled thermometer, is too small to justify the economy.

It is needless to say that a centigrade thermometer should be so accurately adjusted that the zero mark coincides with the height of the mercury column when plunged into melting ice, and that the 100 degree mark should agree with the height of the mercury column when placed in the temperature of steam.

In the modern scientific standardization of thermometers, the range is set between the melting point of mercury (about −40° C.) and the boiling point of sulfur (about 444° C.).

To test thermometers for this purpose is a very simple matter. Such tests should be made from time to time on every thermometer used, as the glass in the thermometer, on aging, undergoes more or less contraction and therefore is apt to become inaccurate. Details of this testing will be found below.

A modification of the thermometer, sold in pharmacies, although not used in pharmaceutic operations, is the well-known fever thermometer. This is generally limited to the temperature of the human body—say from 90° to 110° F. Thermometers of such limited marking can, of course, be made smaller than those of larger scope, hence are more convenient for carrying by a physician.

A popular form of this instrument is the so-called "self-registering thermometer," in which a portion of the mercury rises to the greatest height in the operation, and does not return with the rest of the mercury in contracting, thus leaving a register of the patient's temperature for examination by the physician on his return visit.

This break in the mercury column must be remedied before the thermometer is used for another operation, and this can be done very simply by grasping the thermometer by the upper end, raising same above the shoulder, and giving it a downward circular sweep. This, repeated several times, will remedy the break. The same treatment applies to a chemical thermometer when such a break in the filament occurs.

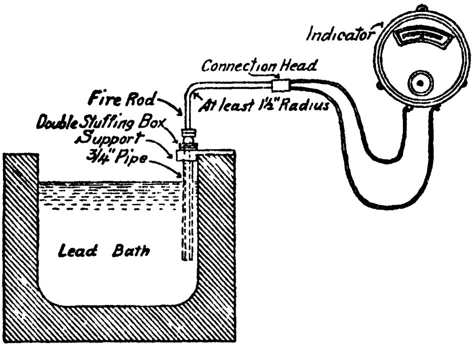


Fig. 53.—Lead bath and pyrometer (for high heat experiments)

In some cases, however, the break is so persistent as to resist these efforts, when it can be brought down by gently warming the thermometer until the mercury rises to the broken part and forces same up, and then shaking the mercury down as above mentioned.

Other Varieties of Thermometers.—In pharmacy the thermometers above mentioned are practically the only ones employed, and to such thermometers the measure of the temperature is limited to minus 40° C., the freezing point of mercury, and to plus 360° C., the boiling point of mercury.

This difficulty has been met in the case of glass thermometers by filling the space above the mercury in the capillary tube with nitrogen under pressure. The increased gas pressure increases the boiling point of the mercury and by this device, mercury thermometers registering up to 625° C. are available. For still higher temperatures, quartz tube thermometers filled with the rare metal, gallium, are available. These register temperatures up to 1800° C.

For very high temperatures, *pyrometers* are employed. The simplest form of pyrometer is the iron bar mentioned on p. 91. In another form the bulb and tube are made of finest porcelain, filled with air, which expands on heating, and the expansion is measured by the pressure of the air on a mercury column.

A more modern form of pyrometer is one in which electricity is employed, this acting on the principle that certain substances on heating show more resistance to electricity than when cold; indeed, in exact proportion to the increase of temperature. Therefore in such an instrument a current of electricity is conducted through the metal, which acts as the thermometer, and the temperature is estimated from the reading of the resistance gauge, or ammeter; the face of which is usually graduated in degrees Fahrenheit or centigrade rather than in amperes (Fig. 53).

LABORATORY EXERCISES

THERMOMETER TESTING

Boiling Point of Water.—Take two thermometers, one with Fahrenheit and the other with centigrade scale. Suspend each in pint flask, which should rest on wire gauze or ring, high enough to permit a flame of Bunsen burner underneath. Have in the flask about 150 cc. of water, and do not let the thermometers dip below the surface of the water.

Apply heat, and when water boils and a goodly amount of steam is passing from the flask, read the height of mercury in each thermometer. The Fahrenheit will read about 210 degrees; the centigrade, about 98 degrees. If much below these points, it is likely due to part of the thermometer being outside the flask and beyond influence of steam zone. To insure full action of steam, the neck of the flask may be lengthened by means of a roll of stiff paper or by inverting over flask a narrow glass percolator. The latter method is, however, not highly satisfactory, first because of danger of cracking percolator; second, because the condensed steam drops on outside of flask.

Note.—Water boils at 212° F. or 100° C. at *sea level*, or at the atmospheric pressure equal to 760 mm. of mercury. (See p. 103.) If the thermometer is tested in a high building or at any place higher than sea level, the boiling point will be less than the standard.

There is no mathematic formula expressing relation of boiling point to atmospheric pressure which can be considered a true law, but Regnault worked out a table of boiling points under different pressures which can here be condensed to the following four lines.

Barometric pressure	*Boiling point of water*
91.92 mm.	50° C.
525.45 mm.	90° C.
760.00 mm.	100° C.
1620.00 mm.	120.4° C.

To this can be added the statement that an ascent of 1080 feet makes a decrease in the boiling point of water of 1° C.

Melting Point of Ice.—Put 4-ounce funnel into iron ring attached to filtering stand and place 2-ounce beaker beneath it. Break ice into pieces about size of a pea, and fill funnel with same. Insert in midst of ice the two thermometers used in boiling point experiment, and let stand five or ten minutes; then take out and read quickly. The Fahrenheit thermometer should read 32°—the Centigrade, 0°.

BIBLIOGRAPHY

Combustion.—(Theory) Smithells, J. Chem. Soc. Trans., 61, 1892, 217; Armstrong, J. Soc. Ch. Ind., 24, 1905, 473; Freund, Chemistry of Combustion (1922); Ubbelohde and Hofsäss, J. Gasbel., through C.A., 8, 1914, 1339; Ubbelohde and Anwandter, J. Gasbel., through C.A., 12, 1918, 1527; Bubinoff, Z. physik. Chem., through C.A., 9, 1915, 995; Anon., Ch. News, 111, 1915, 8. (Temperatures) Wright, Electric Furnaces, 1905; Balliet, Oil and Gas Jl., 23, 1924, 34 (through C.A.); Anon., Jl. Frank. Inst., 205, 1928, 877; Loomis and Perrott, Jl. Ind. Eng. Ch., 20, 1928, 1004; Henning and Tingwaldt, Jl. Soc. Ch. Ind., 48, 1929, 661; Griffiths and Awbery, Jl. Frank. Inst., 208, 1929, 445. (Internal combustion) Brunler, Jl. Soc. Ch. Ind., 44, 1925, 187. (Surface combustion) Kershaw, Met. Ch. Eng., 9, 1912, 628; Bone, Jl. Frank. Inst., 173, 1912, 101; Teclu, J. prakt. Chem., through C.A., 8, 1914, 566; Gray, J. Gas Lighting, through C.A., 8, 1914, 2936; Bradford and Corwin, Power, through C.A., 10, 1916, 382; Anon., Het Gas, through C.A., 18, 1924, 2417.

Baths.—Lippmann, Bull. Assoc. chim. suc. dist., 26, 1908, 790; Meyer, B., 18, 1885, 2999; Sollmann, Jl. A.M.A., 68, 1917, 1895; Benesch, Ch. Zt., 49, 1925, 509. (Wire gauze) Hopkins, J. Am. Ch. Soc., 37, 1915, 321.

Bunsen Burner.—(History) Clark, Jl. Soc. Ch. Ind., 42, 1923, 442A; Hart, Pract. Dr., 46, July, 1928, 19; Griffith, A.J.P., 101, 1929, 803; Clendening, Clin. Excerpts, 5, 1931, 8.

Thermometers.—(History) Fahrenheit, Celsius and Réamur, Ostwald's Klassiker der exacten Wissenschaft.; Anon., Ph. Cent., 30, 1879, 339; Maze, Comp. rend., 120, 1895, 732; Anon., Spatula, 11, 1905, 334; Burgess, C.A., 6, 1912, 2881; Boyer, Jl. Soc. Ch. Ind., 45, 1926, 10; Anon, C.A., 24, 1930, 1251. (General) Häussler, Ch. Zt., 35, 1911, 436; Anon., West. Dr., 28, 1906, 707; Tart. A.Ph.A., 27, 1879, 50. (Pyrometers) Schramm, Eng. Min. Jl., 93, 1912, 355; Anon., Met. Chem. Eng., 13, 1915, 192; Darling, Jakeman and Griffiths, Proc. Phys. Soc., through C.A., 15, 1921, 2753. (Fever) Mayo, Am. Dr., 45, 1904, 255; Anon., Am. Dr., 45, 1904, 409; Bethea, N.O., Med. Surg. Jl., 84, 1931, 130.

Refrigeration.—Killefer, Jl. Ind. Eng. Ch., 24, 1932, 601 and 615; Churchill, *ibid.*, 24, 1932, 623; Waterfill, *ibid.*, 24, 1932, 616; Thompson, *ibid.*, 24, 1932, 620; Pratt, *ibid.*, 24, 1932, 613; Johnson, *ibid.*, 24, 1932, 626; Quinn, *ibid.*, 24, 1932, 610.

CHAPTER V

APPLICATIONS OF HEAT

In studying the dozen or more pharmaceutic processes involving the use of heat, they can be best understood when presented in the following tabulated form:

I. Chemical change in the heated product:

1. Substance is inorganic, is strongly heated, and gives off gas.	(*a*) CO_2 eliminated, *calcination*.
	(*b*) Gas eliminated with a flame, *ignition*.
	(*c*) Gas eliminated with crackling sound, *deflagration*.
2. Substance is organic.	(*a*) Strong heat without access of air, *carbonization*.
	(*b*) Strong heat with access of air, *incineration*.
	(*c*) Moderate heat only, *torrefaction*.

II. Physical change produced in heated product:

1. Solid temporarily changed to liquid, *fusion*.
2. Solid or liquid temporarily changed to gas, *vaporization*.

The modifications of vaporization can best be tabulated as follows:

METHOD	OBJECT SOUGHT	NAME OF PROCESS
Simple vaporization	(*a*) Liquid residue	Evaporation.
	(*b*) Solid residue	Desiccation. Exsiccation. Granulation.
Vaporization and condensation	(*a*) Volatile liquid	Distillation.
	(*b*) Volatile solid	Sublimation.

Discussing the several processes individually we find the following points of interest and importance.

Calcination is the process of strongly heating a carbonate, whereby the gas, carbon dioxide, is driven off and the oxide of the metal remains.

Note the similarity between the words "calcination" and "calx." Calx is the Latin name for lime, calcium oxide, CaO, which is made by strongly heating calcium carbonate, $CaCO_3$, when carbon dioxide, CO_2, passes off. By the identical process—calcination—the oxides of magnesium and zinc are produced, as the following comparison shows:

$$\begin{array}{lll} \mathrm{CaCO_3} & \mathrm{MgCO_3} & \mathrm{ZnCO_3} \\ \underline{-\mathrm{CO_2}} & \underline{-\mathrm{CO_2}} & \underline{-\mathrm{CO_2}} \\ \mathrm{Ca\ O} & \mathrm{Mg\ O} & \mathrm{Zn\ O} \end{array}$$

The results of above subtraction—the remaining oxides—are said to be "calcined."

While the largest operations of calcination are performed in huge plants of masonry called lime kilns or in huge rotary calcining furnaces, in the laboratory the substance to be calcined is usually placed in an evaporating dish (see p. 107) or in a crucible, the source of heat being a blast lamp.

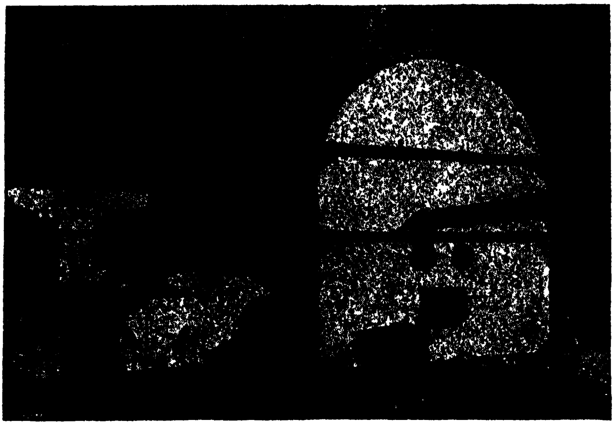


Fig. 54.—Rotary calcining installation used in a cement plant (W. S. Dickie, in Jl. Indust. and Engineering Chem., Vol. 21, 1929, p. 461).

Crucibles are utensils of various sizes, shapes, and materials, according to the objects for which intended. The name crucible dates from the middle ages, when the alchemists (the forerunners of the chemists), in invoking divine aid in their operations, marked utensils of this character with the sign of the cross (Latin, "*crux*").

The modern crucibles are made of the following materials:

Fire clay or *Hessian crucibles* (Fig. 55) are very cheap and convenient apparatus for conducting high heat experiments. They usually come nested, in sizes ranging from 15 to 500 cc. Their chief drawback is that they are poorly annealed, and are therefore liable to break. Moreover, they are too porous to hold water.

Graphite crucibles are more expensive, but are durable. They are commonly called "black-lead crucibles," and are of the same material of which the "lead" of pencils and the cake stove-blacking is composed. They are used more for chemical than for pharmaceutic work, as is also that form of crucible, "the cupel," which is made of bone ash and used exclusively in metallurgy.

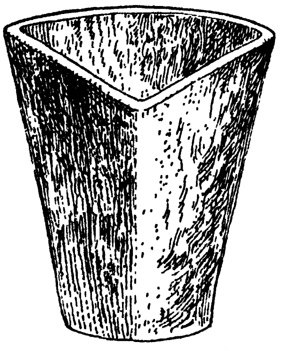


Fig. 55.—Hessian crucible.

Porcelain crucibles are the most popular of all forms of crucibles, being comparatively durable, easy to clean, and moderate in price. They can be obtained in all sizes, but the most convenient are those of 15 to 30 cc. capacity (Fig. 56). *Silica crucibles* (p. 437) are now largely used in chemical work.

Platinum crucibles are too expensive to be of ordinary pharmaceutic use, but the purchase of a platinum crucible is by no means a bad investment, as when the instrument has become worn out, the platinum of which it is composed can be sold at a price but little below its original cost. The most convenient size of platinum crucible is one of 20 cc. capacity. They are of great value, because durable and because possessing powers of resistance against chemicals far greater than other metals. This great advantage must not be abused, however, for it should be clearly remembered that sulfides, hypophosphites, potassium hydroxide and lead salts affect platinum, ruining the crucible in which they are heated.

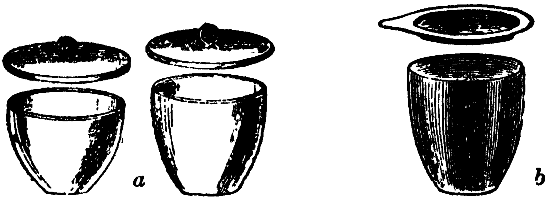


Fig. 56.—Porcelain crucibles (*a*); platinum crucible (*b*).

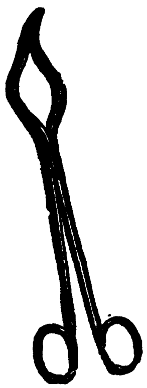


Fig. 57.—Crucible tongs.

Gold crucibles are now available from certain dealers in chemical apparatus. They have little advantage over those made of platinum except that at present the latter metal is more expensive. There is also the danger that the gold may melt at the temperature of the modern Bunsen burner.

Appliances necessary to the successful handling of crucibles are *crucible tongs* (Fig. 57), which are used for lifting crucibles and *triangles* on which they rest while being heated. These, as shown in the illustrations, consist primarily of iron wire covered by clay piping, hence obtainable at small cost. The triangle rests on or is supported by a *tripod* (Fig. 58) or else on the ring of a retort stand.

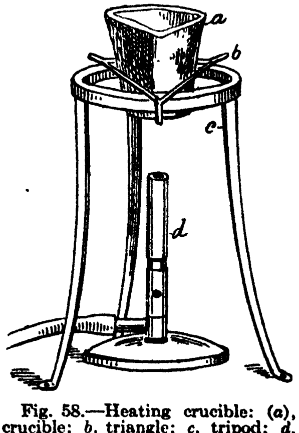


Fig. 58.—Heating crucible: (*a*), crucible; *b*, triangle; *c*, tripod; *d*, Bunsen burner.

Ignition is the process of heating inorganic matter strongly, whereby certain portions are driven off in gaseous forms (frequently with formation of a flame), leaving the nonvolatile residue. This process is used in pharmacy in some analyses, for example: the United States Pharmacopœia of 1890 directed in a test for sulfurated antimony, that the same, on being heated, should lose its sulfur by ignition, leaving a residue consisting chiefly of antimony oxide. In U.S.P. XI, the compounds of bismuth excepting Bismuth and Potassium Tartrate are assayed by ignition (p. 1031). In the chemical industry, ignition is largely employed; for instance in the burning of iron pyrites, when the sulfur which it contains combines with the oxygen of the air to form the gas sulfurous oxide, leaving a residue (ferric oxide) behind.

The ignitions of pharmacy are usually performed on platinum foil, in crucibles, or in evaporating dishes, or even on the end of a spatula or knife blade. Thus the presence of calcium sulfate in a sample of precipitated sulfur is easily detected by igniting a bit of the suspected chemical on the blade of a spatula, when it leaves a residue only in case calcium sulfate is present.

Deflagration is the process of strongly heating a substance readily yielding oxygen, when this element is evolved with a characteristic crackling sound. This phenomenon occurs when potassium nitrate or potassium chlorate is heated, and the process is quite different from that of "decrepitation," which will be explained in the chapter on Crystallization.

Deflagration is used in no process of pharmacy, but it is of value in the testing of some official chemicals, such as potassium nitrate. To produce deflagration the salt is sprinkled on hot coals, or is heated on platinum foil or is placed in a deflagrating spoon (Fig. 59).

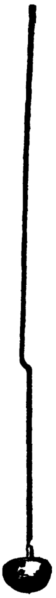


Fig. 59.—Deflagration spoon.

Carbonization is the process of strongly heating an organic substance (that is, a substance containing carbon) in a vessel protected from access of air. Under this treatment the hydrogen and oxygen usually found in organic substances associated with carbon pass off in the form of water, leaving behind the carbon or charcoal.

This process is rarely employed in pharmacy, and when utilized may be performed in a rather tightly covered crucible. The typical example of carbonization is the manufacture of charcoal—"the charcoal burning"—an industry of the well wooded sections of the United States.

If carbonization is carried on in a retort and the volatile products collected, the process is called *destructive distillation*. By such destructive distillation of wood, wood alcohol, acetone, and acetic acid are now made.

Incineration is the process of strongly heating an organic substance with access of air, whereupon the carbon, as well as the hydrogen and oxygen, are dissipated, as oxidation products, and nothing is left but inorganic salts found in the original substance, and commonly called *ashes*.

Incineration is like carbonization, save that the former process is performed in a utensil where the air cannot get at the organic substance, while in incineration the air has full access. This makes the important difference that in carbonization the residue, after heating, is carbon or charcoal and inorganic salts; while in incineration the carbon combines with the oxygen of the air to form the gas, carbon dioxide, CO_2, which passes off, leaving behind only a small residue (ashes) consisting of inorganic salts. Such an operation is illustrated by every open fire; such is the process of cremation. Its use in modern pharmacy is limited to chemical examinations, the amount of ash yielded by drugs being in some cases a valuable criterion of quality. Such ash estimations are performed by carefully drying a crucible by heating in Bunsen burner flame for fifteen minutes, weighing same after cooling in a desiccator (p. 129), carefully placing the drug in the crucible, and weighing, incinerating same, and finally weighing the remaining ash.

In alchemistic times the ashes from certain plants were supposed to be of great value in medicine. Thus the ashes of wormwood, which modern chemistry has shown to consist chiefly of potassium carbonate, was highly esteemed under the name of "sal absinthii," or "salt of wormwood," two synonyms which still cling to the commercial salt.

Torrefaction is the process of more moderately heating organic matter with access of air, in which case the active principles of the substance are not eliminated, but are merely modified. The process is what is commonly called "*roasting*," and a familiar illustration is the roasting of coffee, peanuts, etc. In pharmacy it is an obsolete process, although formerly "*torrefied rhubarb*" enjoyed considerable vogue.

The operation is performed by placing the drug in an evaporating dish, watch-glass, or crucible, and exposing it to a steady moderate heat; best applied by means of a drying oven (p. 128).

Fusion is the process of converting a solid into a liquid by means of heat without the aid of a solvent, the object usually being to enable the straining of the fluid mass or the molding of it to some special shape at the moment of solidification. The process is so well known that it is scarcely necessary to do more than refer to the well-known operation of melting wax as an illustration of fusion. This, therefore, is an official fused substance, as is also the official toughened or molded silver nitrate.

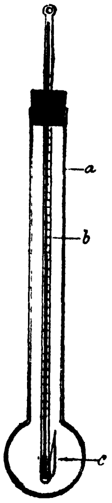


Fig. 60.—Melting point apparatus: *a*, flask; *b*, thermometer; *c*, substance in tube.

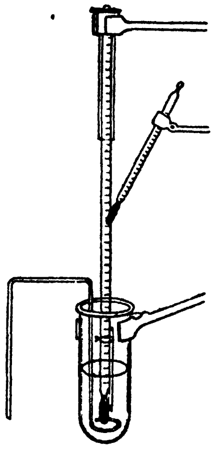


Fig. 61.—Apparatus for taking melting points.

Substances are fused in any appropriate vessel—crucible, test tube, or dish—and the melted mass strained or poured into molds as desired, it being hardly necessary to state that since the liquid returns to solid form as soon as the heated mass reverts to ordinary temperature, the fused condition is merely temporary.

The *melting point* of a substance may be determined by placing the powdered mass in a very small tube, attaching this tube to a thermometer, and immersing the thermometer and tube into concentrated sulfuric acid contained in a beaker or flask (Fig. 60). Heat is then applied to the acid, and the moment the substance fuses, the thermometer is read.

The present Pharmacopœia prescribes (U.S.P. XI, p. 455) very elaborate directions for taking melting points and the illustration (Fig. 61) is taken from that work. The extra thermometer placed above the one used for determining the actual melting point is to note the temperature outside the sulfuric acid, since the upper part of the thermometer is directly exposed to the air and is likely to give faulty results. The factor of correction is also given in the pharmacopœial explanation.

It does not always happen that the temperature at which a solid fuses (the melting point) is the same as the temperature at which the fused material returns to its solid form. This last temperature is called the *congealing point.* Details of estimation of the congealing point are given in the present Pharmacopœia (U.S.P. XI, p. 442).

Vaporization is a general term meaning the change of a solid or a liquid into a vapor; the latter term meaning the gaseous form of a substance, which at ordinary temperatures is either a solid or a liquid.

Liquids and solids are held together by the force of cohesion exerted by their molecules. In gases, the molecules, instead of being held together, actually repel each other; the force of cohesion is practically overcome. To overcome this requires much energy, and it is into such energy that the surplus heat of vaporization is converted. Steam, when placed in a position in which it can gradually assume normal temperature, reconverts into heat the energy necessary to keep its molecules apart, imparts this heat to the surrounding media, and returns to liquid form. Even so do all volatile liquids, and the process whereby a vapor passes into a liquid form is called *condensation.* This condensation is usually hastened, in general practice, by application of cold water or ice to the vapor.

The form of energy necessary to keep the molecules of a substance sufficiently far apart to maintain the vapor form of that substance is called "*latent heat of vaporization.*" Latent heat may be explained as follows: we take a flame that would register 500° C. on a thermometer and put over it a pot of hot water; the temperature of that water will never rise much above 100° C. What then becomes of the surplus heat of the flame? It becomes hidden, it is said; hence the term "latent," from the Latin "*lateo,*" to hide.

But the term is scarcely correct. We learned in Chapter IV that heat was molecular motion—a kind of energy. Now this energy can be transformed into other forms of energy under certain conditions, and that is what happens in the case under consideration.

Water when it reaches 100° C. is converted into steam—it is changed from a liquid to a gas. This transformation means work. It means expenditure of energy, and the energy needed comes from those 400° C. of heat which we say becomes latent.

One of the fundamental rules of physics is that energy is never lost. We may lose sight of it, but it merely assumes another form. Accordingly, all that energy—all those 400 degrees latent heat in the flame—is to be found in the steam, ready for other work, as can be shown as follows:

Take equal parts of water at 100 degrees and at 0 degree and the mixture will have a temperature of 50 degrees, the mean of 100 and 0. Take, on the other hand, equal parts of steam at 100 degrees and water at 0 degree and we get water at 100 degrees. This shows that steam at 100 degrees contains more heat than water at 100 degrees; that this extra heat is used to hold the molecules of the vaporized water apart. The exact quantity of energy has been gaged, and it is found by experiment that 1 part of steam at 100 degrees is not merely capable of raising 1 part of water from zero to 100 degrees, but can actually raise 5.4 pounds of water from zero to 100 degrees. Accordingly, 1 pound steam can raise 540 pounds water 1° C., and we, therefore, say the latent heat of steam is 540 calories (the exact figure is 535.9).

This explains why steam is so much more valuable for heating purposes than an equivalent amount of water at the same temperature, as it also explains why steam is so much "hotter" than water at the same temperature, why a steam scald is so much more painful than a scald from boiling water.

The changing of the liquid into vapor occurs at all temperatures. That water, for example, evaporates freely at ordinary temperatures is demonstrated by the fact that a towel soaked in water and hung in such a position as to allow access of air will readily dry, or, in other words, water will evaporate therefrom. However, water evaporates quickly only when the boiling point is attained.

The **boiling point** is of such pharmaceutic importance that it behooves every student clearly to understand when and how *ebullition*, or boiling, commences.

When a pot of water is on the fire, the first part of the liquid to reach 100° C. is that nearest the flame—at the bottom of the pot. It is, therefore, the water at the bottom that is first changed to steam.

Steam is vapor—a state of aggregation in which the molecules tend to get away from each other. They have overcome the force of cohesion, are wild to break bounds and escape into the open air. This tendency of a liquid to expand to a gas is called the *tension of its vapor*.

The steam at the bottom of the kettle has its tension, but it is restrained in two ways. It has above it the weight of the column of water in the pot, and on top of this the weight of the atmosphere, which presses down with the force of almost 15 pounds to each square inch of surface. Before the steam can escape, before the bubbles of vapor can rise to the surface, the combined restraining power must be overcome by the tension of the vapor of water, and the point where the tension of the vapor overcomes the pressure of the atmosphere is the boiling point, and is attained only at a certain degree of heat absolutely fixed for each liquid.

Vapor may pass off at temperature under the boiling point, but it then passes from the surface of the liquid, with little or no disturbance, and takes place rather slowly.

It is only at that supreme moment—that moment when the heat attained is sufficient to raise the tension of the vapor above the pressure of the atmosphere, that the liquid boils; that bubbles of steam arise from the bottom of the heated liquid.

The statement that a liquid begins to boil when the tension of its vapor is greater than the pressure of the atmosphere can be easily demonstrated by the following experiment:

A glass tube sealed at one end and about 3 feet long is exactly filled with mercury, and inverted into a bowl containing the same liquid. It will be noted that the mercury in the bowl will support a column of mercury inside the tube, usually about 30 inches above its surface. The force supporting the column of mercury 30 inches high is none other than the pressure of the atmosphere on the surface of the mercury in the bowl, and if the area of the interior of the tube be 1 square inch, it will be found that the weight of this 30-inch column of mercury will be 14.7 pounds.

From this we deduce the statement that the usual atmospheric pressure is 14.7 pounds to the square inch, and this has been proved in other ways.

We thus learn what is meant by the pressure of the atmosphere. Now, in order to demonstrate the second part of the statement just given above, that a liquid begins to boil when the tension of its vapor overcomes the pressure of the atmosphere, we insert into the vacuum in the tube above the column of mercury an appropriate quantity of water, which at ordinary temperatures will have but little effect on the height of the mercury column. The moment we begin heating the water a change occurs, the mercury being gradually pushed down toward the mercury in the bowl by the expansive force of the warmed vaporized water; in other words, by the tension of the vapor of the water. As the heat is continued the pressure of the vapor of the water pushes the mercury farther and farther down; in other words, gradually overcomes the pressure of the atmosphere, and this before the liquid begins to boil.

The moment the liquid begins to boil it is observed that the mercury has been completely forced from its former place, that is, the column of mercury 30 inches high has disappeared—the tension of the vapor of water has become equal to the pressure of the atmosphere.

This experiment can be carried on with equal success, with liquids other than water, in which cases it is found that the column of mercury is completely forced down from the barometer at the moment the boiling point of that liquid is reached.

Incidentally atmospheric pressure varies with the altitude and this affects the boiling point of the liquid; the boiling point of water decreasing about 1° C. for each 1080 feet of ascent. Thus in Denver, a city some 5000 feet high, water will boil at 94° to 95° C. and at Leadville, which is some 10,000 feet high water boils at about 90° C. Obviously at high altitudes even as at sea level there is apt to be a continual variation of the atmospheric pressure, so the figures just given are merely averages.

That different liquids possess different boiling points is, of course, too well known to require much comment, but mention may be made that while water boils at 100° C., alcohol boils at 78° C., chloroform at 61° C., and ether at 35° C.

Estimation of boiling point is discussed on p. 96. An elaborate method of estimating the boiling point is given in the present pharmacopœia (U.S.P. XI, p. 439).

As shown in the table given on p. 97, there are several modifications of vaporization, all of which will now be discussed.

Evaporation, in the strict sense of the word, means the vaporization of a liquid from a liquid, as, for example, the removal of alcohol from water by gentle heat. In a broader sense of the term, however, it includes the removal of liquid by heat from any solution. Thus it is more usual to speak of evaporating a solution of salt than of evaporating alcohol from water.

Conditions Affecting Evaporation.—The rapidity of the evaporation depends rather largely on the following conditions:

First, *amount of heat.*

The greater the source of heat, the more rapidly the evaporation will take place.

Second, *the amount of atmospheric pressure.*

As noted above, the less the atmospheric pressure, the lower the temperature necessary to bring the liquid to the state of ebullition. Thus, while water boils at the ordinary atmospheric pressure of 14.7 pounds to the square inch, at 100° C., the same water, placed in a container from above which the pressure of the atmosphere has been lessened to 1.7 pounds to the square inch, will boil at 50° C. On the other hand, the same water confined in a strong closed vessel of metal, known as an autoclave (Fig. 178), can be heated above its boiling point under pressure. If the pressure on the surface of the liquid is 100 pounds to the square inch, the water will not boil until the temperature of 164° C. is reached.

Many cases of evaporation are carried on in special apparatus in which the atmospheric pressure has been lessened, such apparatus being called vacuum pans.

Third, *amount of humidity in the air.*

An aqueous solution, on evaporating, is converted into steam which, of course, passes off into the atmosphere, and the rapidity with which the air receives this vapor is in proportion to the amount of moisture already contained in the atmosphere. A dry air naturally absorbs more moisture than will a humid atmosphere, hence liquids evaporate more rapidly in dry air than in humid air.

Fourth, *character of the solvent.*

In evaporating liquids at the boiling point, the nature of the solvent influences to a greater or less degree the rapidity of evaporation: a thin mobile liquid usually evaporates more rapidly than a dense and viscid liquid. The question of evaporation is not, however, a mere question of relative specific gravities, as is shown by the fact that the very volatile chloroform (boiling point, 61° C.) is one and one-half times heavier than water, the volatility of the chloroform being due to the mobility of the liquid and not to its density. The reason a mobile liquid evaporates more readily than does a viscid one is because its molecules, having little adhesion, freely separate from one another, thus affording the exit of the vaporized portion. In the case of viscid liquids, like syrup or mucilage of gum arabic, the molecules do not freely separate from one another, and on evaporation of such liquids this fact can be noted by examination of the bubbles formed as the liquid vaporizes.

The influences affecting evaporation by boiling and evaporation below the boiling point are of different character, in the first case the main factor being the extent of surface exposed to the heat, while in the latter case it is the extent of surface exposed to the air; hence each of these can best be considered separately.

Evaporation by Boiling.—Since heat is necessary to facilitate boiling, it follows that the greater the surface exposed to the source of heat, the more rapidly the liquid will boil, and this result is obtained not simply because of such broadening of the surface exposed to the heat, but also because of the fact that such broadening implies a corresponding decrease in the depth of the liquid. As an illustration, the volume of 100 cc. water will have much less depth if poured into a flat dish than if retained in a graduate, and that the lessening of the depth facilitates ebullition can be understood when the fact is noted that the liquid begins to boil not merely when the tension of its vapor is greater than the pressure of the atmosphere, but when such tension is greater than the pressure of the column of the liquid above. Hence in evaporating at boiling we try to place the liquid in as thin a layer as possible, by choosing flat forms of evaporating dishes and the like.

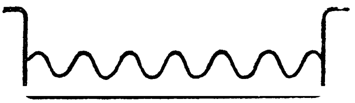


Fig. 62.—Corrugated pan bottom.

Since evaporation by boiling is influenced by the amount of surface exposed to the heat, the character of the vessel plays its part, as certain materials and certain shapes transmit heat better than others. Thus iron and copper vessels are better for evaporation of liquids than are porcelain, because of the greater conductivity of the metals. This statement, however, does not mean an unqualified recommendation of iron and copper utensils for evaporation of pharmaceutic products, as the question of preserving the purity of the chemicals is of far more importance than is the rapidity with which it can be evaporated, and metallic vessels are very apt to contaminate the products.

As to form, a corrugated vessel will transmit heat more readily than a flat-bottomed one, as is self-evident by examination of Fig. 62, where it is seen that a corrugated vessel actually exposes about twice as much surface to the heat as a flat-bottomed vessel of the same diameter.

In the same way a liquid will evaporate more readily in a rough vessel than in a very smooth one. For this reason in boiling water for domestic purposes a rough iron kettle is preferred, as the roughness of the utensil acts the same as does the corrugated bottom of the ideal evaporating vessel mentioned above. The external roughness and lack of luster of the vessel is also a contributing factor, inasmuch as finely polished external surfaces act as reflectors of heat as well as light, actually throwing off the heat instead of transmitting it to the interior; hence, the making of boilers and kettles with rough and dark exteriors.

Evaporation Below the Boiling Point.—While in this case of evaporation more attention is paid to the surface exposed to the air than to the surface exposed to the heat, and the two usually resolve into the same thing, because in obtaining the largest surface exposed to the air we use a shallow vessel, even as we do in attempting to increase the surface exposed to the heat.

The pharmaceutic application of evaporation below the boiling point is generally limited to the desiccation of substances and the evaporation of liquids which are apt to be decomposed when heated on a wire gauze, and, therefore, directed to be heated on a water bath. While a water bath itself has the temperature of 100° C., it never transmits that heat to the substance placed on same. The actual temperature of a liquid heated on a water bath is usually from 90° to 95° C., the surrounding air causing that much loss of heat when transmitted from the water bath to the substance. For this reason an aqueous liquid cannot be made to boil in an ordinary water bath and, therefore, the evaporation of such aqueous liquid on a water bath is a rather tedious matter. The evaporation can be facilitated by constant stirring, this stirring producing the same effect on the liquid as the corrugated bottom of the evaporating dish mentioned above, by increasing the extent of surface exposed to the heat. Stirring the liquid produces waves thereon, and as a wave in its ideal sense represents a corrugation, it means an increased surface exposed to the air. To attempt to evaporate an aqueous solution on a water bath without constant stirring is practically useless.

Evaporation can also be hastened by blowing heated air upon the surface of the evaporating liquid.

Kober has found that a solution suspended in air in a bag made of evaporated collodion rapidly evaporates. In such a bag a solution of serum albumin was evaporated to complete dryness at 37° C. in twenty-four hours. Kober calls the phenomenon *perevaporation.*

In some cases liquids are evaporated without recourse to any ordinary heat, that is, at the ordinary temperature, and such is called spontaneous evaporation.

Spontaneous Evaporation.—An illustration of this is seen in the drying of clothes when the same are spread to their utmost extent and suspended from lines, thus increasing the surface exposed to the air. Applications of this principle are comparatively limited in pharmacy, as in most cases the ordinary sources of heat are generally cheap enough to permit their use in evaporation.

Two cases, however, in which spontaneous evaporation is used commercially may be cited. In the first case, in Germany, salt is extracted from the water of certain springs by this process with profit, where evaporation with ordinary fuel would not pay. In such process the water is allowed slowly to trickle through wooden frames about 30 feet high and many feet long, filled with straw and twigs. This framework has no sides, thus affording a thorough circulation of the air, and as the liquid trickles through the frame, enough of the water is evaporated to cause it to reach the bottom trough sufficiently concentrated to justify using heat for the final evaporation.

Another case of spontaneous evaporation, applied commercially, is the evaporation of sea water practiced in Portugal and Spain, where direct solar heat is utilized for evaporation.

In this case the solution is pumped into shallow ponds and allowed to stand exposed to the sun's rays for three or four weeks, when sufficient evaporation will have occurred to bring about the crystallization of the salts.

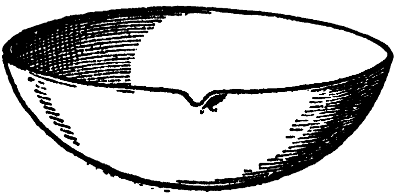


Fig. 63.—Evaporating dish.

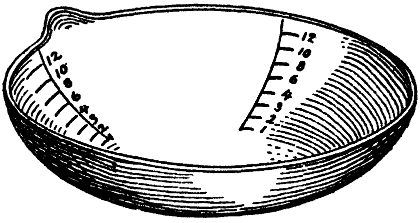


Fig. 63a.—Evaporating dish, graduated inside.

Evaporating Apparatus.—The articles essential to evaporation in pharmacy are dishes and stirring rods and the appropriate sources of heat. Other apparatus used in the technic and of advantage in pharmacy, though not essential, are fume closets and hoods, grommets, and the very useful but expensive vacuum apparatus.

Evaporating Dishes.—These are made of porcelain, glass, silica ware (p. 437) or platinum, shallow vessels of the appearance shown in Fig. 63. For practical purposes the porcelain dish is generally preferred, being more durable and comparatively inexpensive. Glass evaporating dishes are too fragile for continued use, and are chiefly used in crystallization. Silica dishes are now purchasable at reasonable prices and have many advantages. Platinum evaporating dishes are used in some chemical operations, their expense precluding general use.

Other metals are not useful in making evaporating dishes and even enameled dishes should be used with great caution in pharmaceutical evaporations because of danger of contamination of the evaporating fluid. On the other hand, for chemical manufacturing on the large scale special evaporating apparatus lined with special types of enameling are used with conspicuous success.

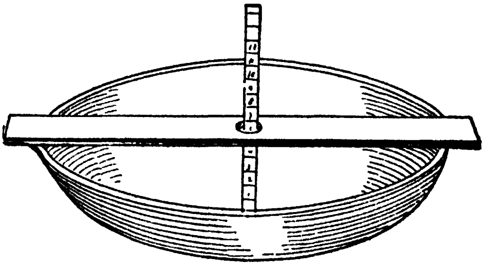


Fig. 64.—Evaporating dish, graduated with stick.

In some cases of evaporating directions are given to "reduce" the liquid "to a certain bulk," and for this purpose graduated evaporating dishes have been introduced (Fig. 63*a*).

Instead of same, however, a home-made contrivance answers just as well, and this consists of a rod or cylinder of wood, measuring the volume by marking same on the stick (Fig. 64).

To avoid the necessity for these graduated evaporating dishes recipes frequently direct that such evaporations to be conducted until the liquid is brought to a definite weight, in which case the evaporating dish is transferred from the source of heat to the scales. Of course, in order to learn the weight of the liquid the weight of the evaporating dish itself, "the tare," must have been previously ascertained. It is a good practice to tare each dish when obtained, and mark the tare in lead pencil on the outside.

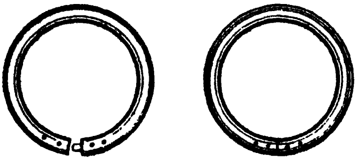


Fig 65.—Grommet.

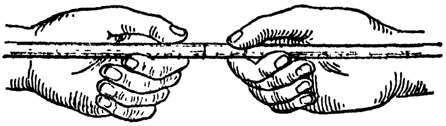


Fig. 66.—Breaking glass rod.

An important point to remember is that a porcelain dish should never be heated in direct flame, the source of heat being modified either by use of the wire gauze or by disks of asbestos.

A warm evaporating dish should never be placed directly on a counter. If the counter is of wood, the heat may be sufficient to soften the varnish. and if it is of metal or marble, the rapid chilling of the evaporating dish, through the difference in its temperature and that of the surface of the counter, may cause a fracture of the dish. It should, therefore, be placed on a mat, or, better, on a "*grommet,*" the latter consisting of a rubber ring the construction of which is shown in appended sketch (Fig. 65).

Stirrers.—The stirring of an evaporating liquid is a valuable aid to rapid evaporation; hence the use of stirrers. Their construction depends on the uses for which they are intended. Thus, in large operations, such as evaporating infusions of drugs containing no acid, a large tin spoon is as valuable as a stirrer. In other large operations, such as making syrups, a wooden paddle answers. For the more delicate operations of pharmacy and chemistry glass rods are required, which can be obtained in various diameters from chemical apparatus manufacturers in 3- or 4-foot lengths, and then can be readily broken by scratching with a file and applying pressure on either side of the scratch, thus fracturing same, as shown in Fig. 66.

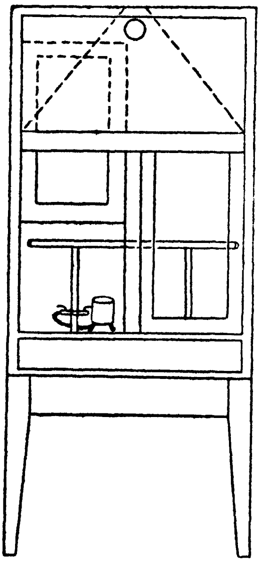


Fig. 67.—Fume closet.

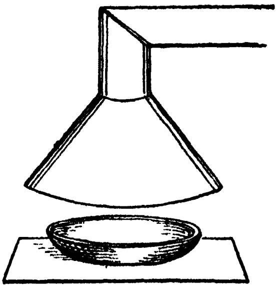


Fig. 68.—Hood.

In cutting these stirring rods it is best to make them of such length that about two thirds will rest within the container for which intended. If more than a third projects over the outside, they are apt to be top heavy. After breaking the rod to the appropriate length, the rough edge should always be smoothed by rotating in a Bunsen flame until slight fusion is effected. If the rough edges are permitted to remain, there is danger of scratching the interior of the evaporating dish.

Fume Closets and Hoods.—Evaporation of a large quantity of liquids, and particularly the evaporation of liquids yielding disagreeable or corrosive vapors, in a closed room is objectionable, and to carry off these vapors fume closets and hoods have been devised. The principle of these two is the same, both being an inclosed space connected with a flue or chimney, through which there is sufficient current of air to draw off the offensive vapors. The closet is a large piece of furniture constructed of wood and glass, and attached directly to the wall (Fig. 67). For a hood can be utilized appropriate lengths of stovepipe, the lower end of which is arranged around a metallic dome, directly under which is placed the evaporating liquid (Fig. 68). Hoods work best if connected with a suction pump.

Fig. 69.—Stokes' vacuum still with condenser.

Vacuum Apparatus.—The principle of the operation of a vacuum apparatus having been explained, it is necessary here merely to state that many organic substances, when evaporated even at water bath temperature, will dissociate. Thus, if sugar is evaporated even at the heat of 100° C., the brown substance, molasses, is produced with accompanying vitiation of the finished product. For all such cases vacuum evaporation is desirable, and this is performed in a suitable evaporating utensil, usually heated by the steam coil, and connected with a dome apparatus which, in turn, is connected with an appropriate vacuum pump (Fig. 69). From the illustration it will be seen that the vacuum pan is connected with a worm condenser (p. 115), thus permitting the recovery of the solvent, if it is costly. This is usually the case when vacuum evaporation is employed in pharmaceutical manufacturing.

where it is chiefly used in the concentration of alcoholic percolates, such as in making extracts (p. 296). As seen in the illustration, the air is exhausted by means of a pump operated by steam or electric power. In the technic such evaporating apparatus is largely used, and for pharmaceutic and chemical purposes a small and comparatively inexpensive apparatus of the same character has been devised (Fig. 70).

For removing atmospheric pressure, any form of air pump can be used, but usually in laboratory work the water suction pump (Fig. 71) is employed. This can be attached to the ordinary hydrant, provided the water pressure is sufficient. In this simple and useful apparatus the rapid flow of the water through a narrow point draws with it the air from the tube and from the connected aspirator, and if the water pressure is sufficient, a vacuum of 17 mm. can be readily obtained. By a vacuum of 17 mm. is meant that the height of a column of mercury supported by the atmosphere is reduced from 760 to 17 mm.; the latter figure, therefore, showing a pressure of only $^{17}/_{760}$ of the ordinary atmospheric pressure. The indication of this pressure is accomplished by the instrument called the manometer. Some forms of manometer are delicate apparatus made on the principle of the steam gage, but for chemical work a simple manometer consisting of a bent tube (Fig. 72) filled with mercury, and set up against a scale, answers all purposes.

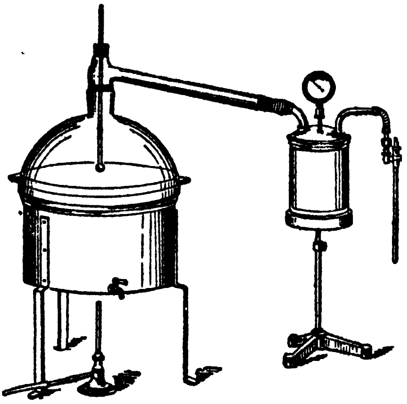


Fig. 70.—Pharmaceutic vacuum pan.

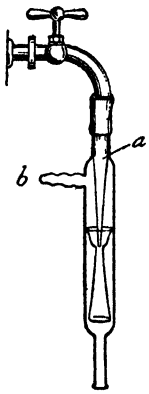


Fig. 71.—Water suction pump: *a*, water tube; *b*, air tube.

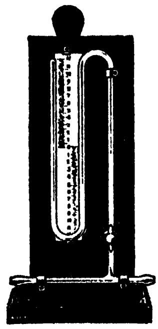


Fig. 72.—Manometer.

The simple form of such vacuum evaporating apparatus is that figured in vacuum distillation (p. 122).

Other Methods of Evaporation.—In some cases even vacuum evaporation does not work satisfactorily and many ingenious schemes have been devised, such as (in evaporating milk) spraying the fluid into heated room, when the water passes off as steam and the solid falls on the floor as a powder and (in evaporating rubber latex) spraying upon a rapidly revolving warm disk. The latter process is employed to some extent in concentrating phosphoric acid (see p. 451).

In large chemical factories, elaborate types of evaporating and condensing apparatus are employed. For these the reader should consult books on technical chemistry.

DISTILLATION

Distillation is the process of converting a liquid into a gas, and condensing the gas back into a liquid.

Objects.—In distillation we have an admirable method of purifying volatile substances. If such a liquid contains impurities less volatile than itself, the impure product is placed in a still and heated, whereupon the substance desired will distil, leaving the less volatile substance behind. In many cases the foreign matter is water, in which case distillation is of great value in strengthening the product under consideration. This is particularly the case in a separation of alcohol from whisky or other alcoholic liquors, which is always accomplished by distillation. The liquid thus purified by distillation is called a "*distillate.*"

In other words, distillation is evaporation of a liquid and subsequent condensation of its vapor. Evaporation has been described on a preceding page, and here it is necessary to turn attention only to the second part of the process, namely, condensation.

As already learned, to convert a liquid into a vapor means the expenditure of considerable energy, which energy is obtained from a source of heat, this heat being converted into the other form of energy (that necessary to keep the molecules of the gas separate from one another) is no longer indicated by means of the thermometer, and such heat is called "latent." If the converting of the liquid into a vapor means the expenditure of considerable heat, so in the inverse operation of changing the vapor back into a liquid an equal amount of heat is given off. In other words, heat is rendered latent in converting a solid into a liquid or a liquid into a gas, and, in turn, latent heat is rendered sensible by changing gas back to liquid, or liquid back to a solid form. Therefore to condense a vapor back to liquid form the chilling of the vapor is necessary, that is, the latent heat must be absorbed by being brought into contact with a cooling agent. The converting of the vapor back to the liquid form in condensing can be accomplished in many cases by bringing the vapor in contact with chilled water.

The amount of water required can be figured out mathematically, and depends on the temperature of the vapor and the temperature of the water before and after its use as a condensing agent. Thus, 1 kilo of steam at 100° C. will take 23.2 kilos of water at 20° C. for condensation, and the temperature of the water after condensation will be 45° C., or 1 kilo of steam at 100° C. will take 24 kilos of water at 10° C., heating it to 35° C. during condensation.

The **apparatus** required for distillation consist primarily of a *boiler*, in which the liquid is vaporized, and the *condenser*, in which the vapors are chilled until they are condensed to the liquid form. This combination of boiler and condenser is commonly called the *still*, and the many forms of this apparatus which are in use can be roughly divided into two classes—the alembic form and the retort form.

In the alembic form the condensing apparatus is directly over the boiler, while in the retort form the condensing apparatus is placed on one side of the boiler, thus not directly over the source of heat. The retort form of a still being more commonly used, it will be discussed first.

Retort Still.—So called because the original form of boiler for such operation was the glass instrument called a retort, which consisted of a glass flask with a long and tapering neck, bent at an acute angle. This simple form of retort is inconvenient by reason of the difficulty in filling such a retort, it being, of course, essential to secure a pure distilled product that the neck of the retort through which the distilling vapor passed should be free from impurities.

Therefore, the charging of such a retort must never be done by pouring the liquid down the neck, but the liquid must be introduced into the bowl of the retort by means of a funnel with a long tube connected therewith (Fig. 73).

Of greater convenience is the tubulated retort, the use of which is strongly urged in preference to the plain form. In purchasing such a retort be sure, however, that the tubulure is correctly placed, namely, directly over the bottom of the bowl, for, if the tubulure is placed otherwise, there is danger of spattering the neck of the retort with the impure liquid when it is poured in (Fig. 74).

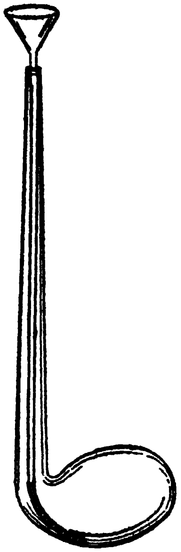


Fig. 73.—Charging plain retort.

For the purpose of insuring the cleanliness of the neck of the retort care should be taken to select such having an acute bend. In retorts where the bend is round rather than acute, there is always danger of some of the liquid being drawn over the bend by capillary attraction into the neck of the retort. Retorts formerly had extended use, but at present they are in less demand and have been largely replaced by the more convenient and simple instrument, the distilling flask (Fig. 75), which consists of a chemical flask of required size, provided with a cork stopper through an orifice of which passes a piece of bent glass tubing. In many cases a second hole is bored through the cork for the insertion of a thermometer. Details of fitting the connections will be given later. A more compact form of distilling flask for small operations is shown in the illustration here given (Fig. 77).

All-glass distilling apparatus with ground-glass joints and mercury seals are now available for laboratory use. Distilling apparatus of silica ware (p. 437) is also available, the distilling flask (or retort) being made as large as 75-liter capacity (Fig. 78).

Condensers.—The condenser is the part of the apparatus in which the vapors are converted into a liquid, and consists of an appropriate container which can be kept cooled by means of ice or running water.

The simplest form of condenser is a *receiver*, which, in many cases, consists of a chemical flask resting within a basin, in which water or ice can be placed. The more elaborate forms of receivers, the tubulated and quilled, are shown in Fig. 79.

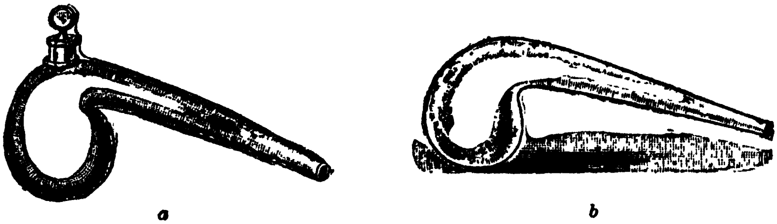


Fig. 74.—Retorts: *a*, tubulated; *b*, plain.

The receiver is the only form of condenser necessary for liquids boiling above 150° C., in which case the temperature of the atmosphere is sufficiently below the temperature of the boiling liquid to permit its use for condensing purposes. In most cases, however, it is usual to have the

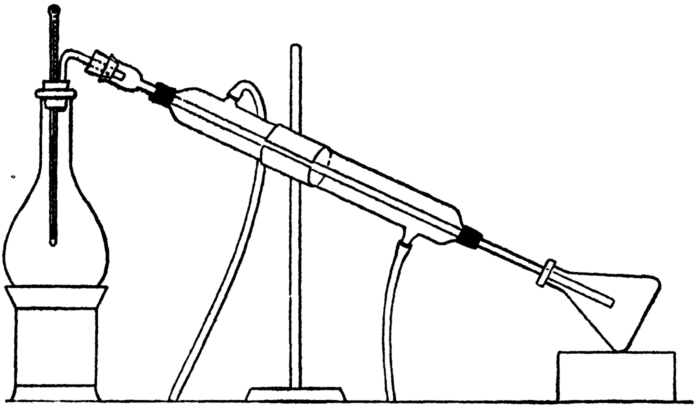


Fig. 75.—Flask distillation.

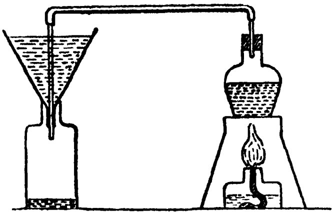


Fig. 76.—A simple distilling apparatus

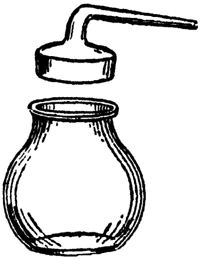


Fig 77.—Glass-stoppered distilling flask.

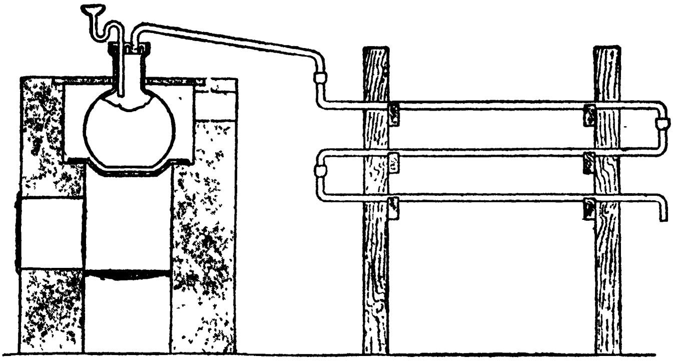


Fig. 78.—Silica ware retort and condenser.

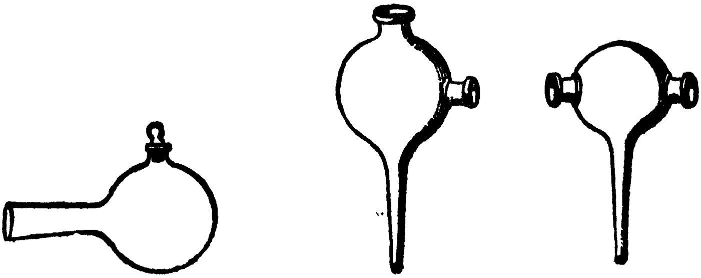


Fig. 79.—Receivers: *a*, tubulated; *b*, quilled.

receiver immersed in water, as mentioned above. In distilling liquids boiling below 150° C., such as water or alcohol, the air is not sufficiently cool to act as a perfect condenser, and in such cases cold water is usually substituted, it being convenient to arrange a continuous stream of water by connecting the condenser with a hydrant. In cases where a hydrant is not convenient, a stream of running water can be maintained by placing the water in a container several feet above the condenser, and maintaining a continuous stream over the condenser by means of the syphon. In such cases of water condensation, preference is usually given to the Liebig condenser.

Liebig Condenser.—This consists of a long glass tube which is connected with the boiler, be it a retort or flask, thus affording passage to the vapor arising from the boiler. Surrounding this glass tube is a second tube, either of glass or metal, through which passes a stream of cold water (Fig. 80).

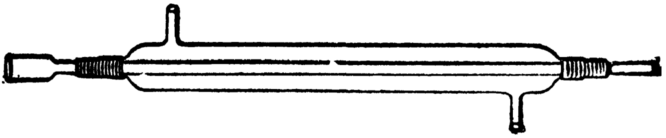


Fig. 80.—All-glass Liebig condenser.

In the typical form of Liebig condenser the outer glass tube has fused thereto ingress and exit tubes, and both ends of the cylinder are tapered so that the joint between the inner glass tubes and the condensing cylinder is made water tight by means of rubber tubing.

Such condenser, while handsome, is rather fragile, because the projecting ingress and exit tubes are apt to be broken off, with resulting fracture of the glass cylinder. Therefore, of far more practical use is the simple home-made condenser, consisting of a central glass tube passing through two corks, which effectually close the outer cylinder of uniform caliber. Through each of these corks passes an ordinary piece of glass tube, which serves as an entrance and exit tube for the water (Fig. 81).

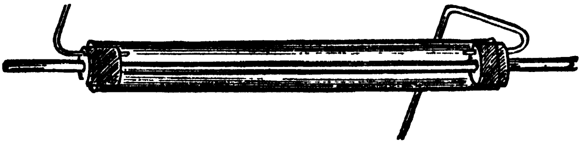


Fig. 81.—Corked Liebig condenser.

In this case the outer cylinder can be made either of glass or metal, and a very effective form of condenser can be made by using, as the outer cylinder, the ordinary tinned iron plaster box.

Should the condensing tube become dirty, it can be washed with soap and water and scrubbed by passing through the tubes a plug of cotton attached to a stick or rod.

The only objection to the condenser just described is that the condensing tube, in order to be effective, must be of considerable length, say 3 or 4 feet, and accordingly occupies considerable space when the apparatus is set up. In large processes of distillation, such as the manufacture of alcohol, a much longer condensing surface is required, and to make an effective straight condenser, taking, say, 30 feet, is hardly to be considered by reason of the space it would necessarily occupy.

This gave rise to a modification which answers the double requirement of occupying small space and of affording a large condensing surface.

The Condensing Worm.—This consists of a tube of glass or metal (usually block tin), twisted into a spiral and fitting into a vessel through which water can circulate freely. Such form of worm is used for all the large processes of distillation, such as obtaining alcohol and alcoholic liquors and distilling volatile oils. An objection to the worm, from the pharmaceutic standpoint, is the fact that its spiral form renders a thorough cleaning very difficult.

In technical operations a worm is used continually for the distillation of one substance, in which case a thorough cleaning is rarely needed, and this is accomplished by running water and other appropriate solvent through the tube. A combination of worm and Liebig condenser is shown in Fig. 82; it has value in a well-equipped organic laboratory, but is of little use in pharmacy because of difficulty of cleaning.

Distilling Appliances.—In performing distillation with flask or retort and condenser, the fitting of the apparatus is a matter of considerable skill, and requires appliances not yet mentioned.

Glass tubing is usually needed to complete the connections, and a stock of good tubing should be at the disposal of every pharmacist, and with the manipulation of same he should be thoroughly acquainted. Such tubing comes in lengths of 3 or 4 feet, and can be easily broken into required lengths in the same way as glass rods, and, as in the case of glass rods, the edges should always be rounded by holding in a flame.

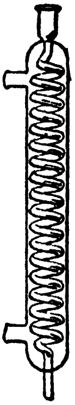


Fig. 82.—Spiral condenser.

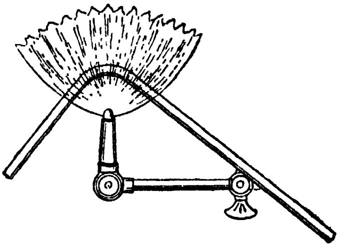


Fig. 83.—Bending tubing.

In bending glass tubing best results are obtained by first grasping one end, holding the tube over a fish-tail flame in such way that the end held by the hand is nearer the flame than is the other end. Rotating in the flame is not necessary, for, when sufficiently softened, the tube bends by its own gravity, and a round, smooth curve is obtained (Fig. 83).

The glass tube bent, the same must be inserted through the cork, which means that the holes must first be bored through the cork. This is done either by a rat-tail file (Fig. 85) or by a cork-borer, a set of hollow brass tubes with lower end sharpened (Fig. 84), and the latter does the work so much more neatly that its use is strongly recommended.

To hold the condenser and the flask in place, we use clamps attached to a *retort stand*, a piece of apparatus of great value in all the operations described in this chapter, consisting, as it does, of support with clamps for condensers and rings for holding dishes during evaporation or percolators or funnels (Fig. 86). In the absence of such a stand the ingenious and economic pharmacist can easily make an appropriate holder for his condenser from a wooden box, as shown in Fig. 87.

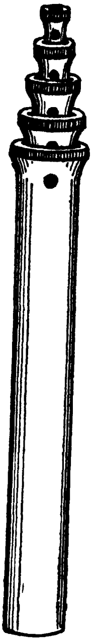


Fig. 84.—Cork borers (nested).

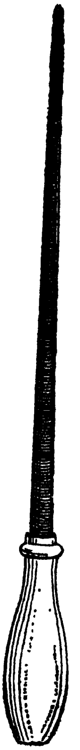


Fig. 85.—Rat-tail file

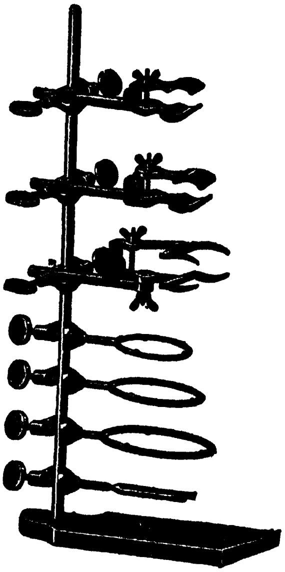


Fig. 86.—Retort stand.

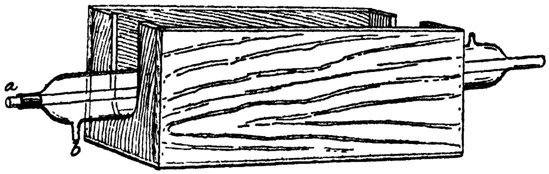


Fig 87.—Box condenser holder.

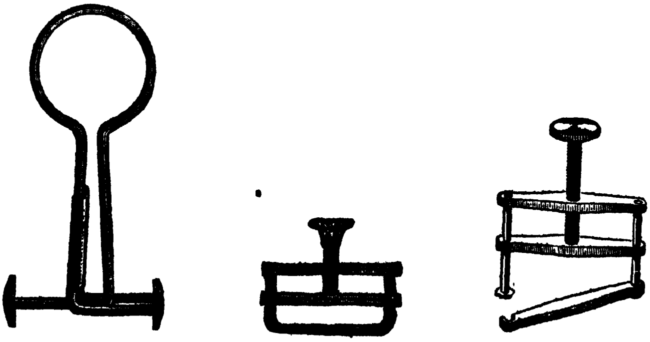


Fig. 88.—Pinch cocks.

In connecting the condenser with the water mains, rubber tubing is essential, and very convenient for regulating the flow of water are the *pinch cocks* which slip over the tubes and which can be opened or closed as shown in Fig. 88.

In making the connections between retort and condenser, rubber tubing is equally useful, although in processes requiring careful distillation contact of the vapor with rubber tubing should be avoided as much as possible, in all cases it being advisable to have the glass tube from the retort introduced into the condensing tube (Fig. 89). The neck of most large retorts is usually larger than the opening of the condensing tube, and in such case, in order to avoid recourse to direct rubber connections, *adapters* are used, these consisting of tapering glass tubes which complete the "all-glass" connections between the retort and the condenser. For adapters nothing is better than the neck of a broken retort (Fig. 90).

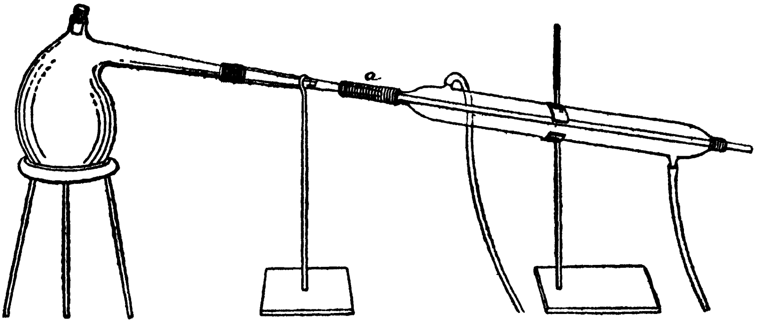


Fig. 89.—Fitting retort to condenser: *a*, flaxseed lute.

In some cases of distillation care must be taken to prevent the pressure of the vapor from producing a fracture of the distilling apparatus, or even explosions, and for such purpose safety tubes or funnels are used, as seen in Fig. 91. Those used in chemistry consist of a bent thistle funnel, in the elbow of which a few globules of mercury are placed, thus producing sufficient pressure to prevent a needless escape of the vapor, by being thrown up into the thistle bulb when the pressure within the flask becomes dangerous.

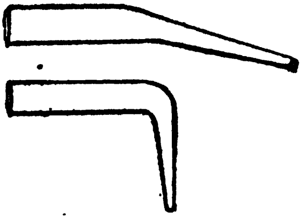


Fig. 90.—Adapters.

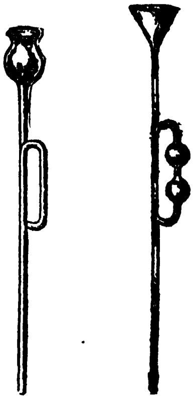


Fig. 91.—Safety tubes.

Bumping.—This phenomenon is a disagreeable accompaniment of many cases of distillation occurring in a flask. In some cases the liquid does not boil steadily under application of heat, but at times the ebullition ceases for a few moments, then suddenly resumes, with a force sufficiently explosive to cause a spattering of the liquid, if not a fracture of the flask.

Bumping occurs chiefly with heavy and somewhat viscid liquids, which cause a retention of generated steam until a sufficient quantity has been formed to force its way through the opposing medium.

To eliminate this phenomenon, which very frequently spoils a tedious distillation by spattering some of the impure liquid into the condenser, and thence into the distillate, means to distribute the heat uniformly, and the insertion of pieces of pumice stone, glass, or platinum has been suggested. None of these, however, answers as well the maintaining of a minute current of steam or air through the distilling liquid.

Alembic still is that form in which the condenser is directly over the boiler, and while the liquid distils more slowly in the alembic than in the retort form, it gives a purer distillate, as there is no danger of any of the liquid being carried over mechanically. A good commercial type of this form of still is the Phœnix condenser (Figs. 94 and 95).

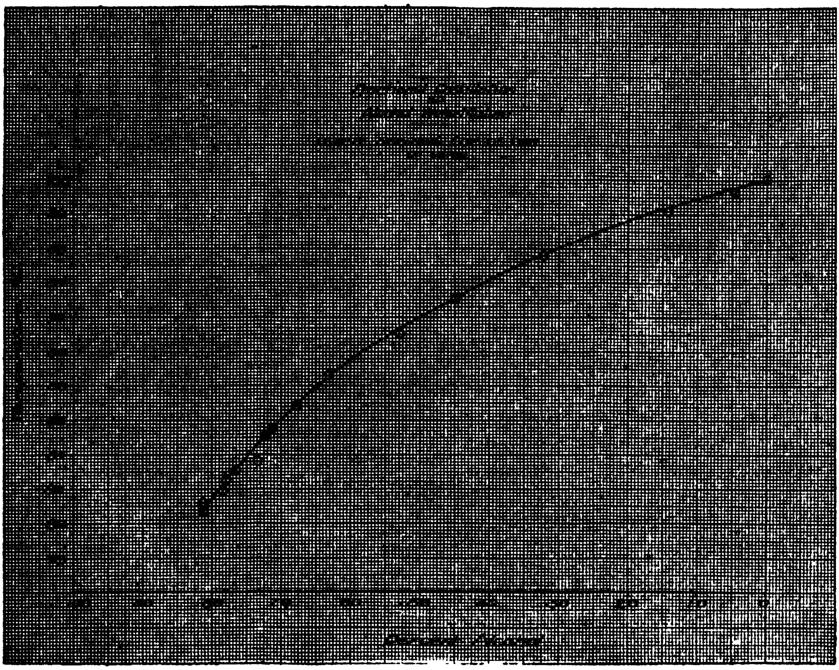


Fig. 92.—Graph of alcohol distillation.

Modifications of Distillation.—*Fractional distillation* is the method used for separating a mixture of several liquids of different boiling points. Assuming, for example, we have a mixture of ether, boiling point 35° C., chloroform, boiling point 61° C., and alcohol, 78° C., it would seem easy to separate them by placing in a flask connected with a condenser and having a thermometer inserted in its neck, and gradually applying heat. When the temperature of 37° C. is attained, the ether should all distil over and be collected. Raising the temperature to 61° C., that portion should all distil over and be collected in a separate container, and, lastly, by raising the temperature to 78° C., the residue, which should consist entirely of alcohol, should distil over and be collected. However, the process is by no means as simple as this, for the reason that while it is true a liquid does not boil until a certain temperature is attained, the vaporization of that liquid occurs at temperatures other than its boiling point, and, accordingly, the first distillate we obtain contains alcohol, chloroform, and ether, and likewise the second and third distillates contain some traces of ether, which had not been fully vaporized at the lower boiling point.

Therefore, in order to carry out the distillation thoroughly, it is necessary to take the three distillates we have obtained and redistil them, and experience has shown that in most cases a second repetition of the experiment will finally yield products which are practically chemical entities.

This process of repeated fractional distillation is largely used in chemistry, although scarcely at all in the ordinary pharmaceutic operations. By this means we are able to separate the volatile oils into their many constituents, and the same process is used for the separation and purification of the petroleum products.

Physical chemists have shown that the problem concerns the tension of the mixed vapor and they have been able to plot out curves showing the successive boiling points of such mixtures. Figure 92 shows the "graph" for alcohol and water mixtures. Checking up the dots on or near the curve, we find that when the thermometer in the upper part of the still (not immersed in the liquid) registers 82° C., the strength of the alcoholic distillate is 78.5 per cent that when the temperature is 85° C. the alcoholic strength is 72.4 per cent; that when the temperature is 91° C., the alcoholic strength is 53 per cent; that when it is 100° C., the alcoholic strength is 0.0 per cent. In the same way the twelve other readings can be readily deduced from the chart.

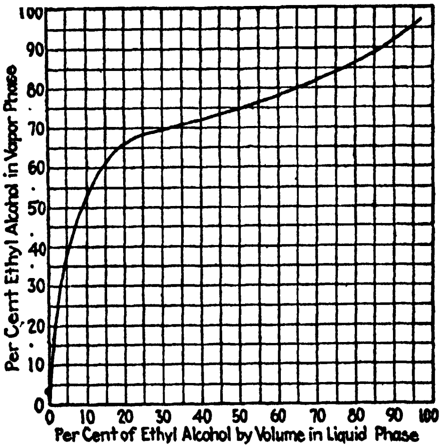


Fig. 93.—Equilibrium concentrations of liquid and vapor phases, ethyl alcohol under atmospheric pressure.

Winter has pointed out that an important factor in plotting a graph such as the one just given is the percentage of alcohol in the liquid phase; the illustration just given showing the results upon distilling a 50 per cent alcohol. For other alcoholic strengths, Sorel's table comes into play and this variation is expressed on the graph given above (Fig. 93).

This graph shows that 10 per cent alcohol gives a vapor containing 51 per cent of C_2H_5OH; that 20 per cent alcohol gives a vapor containing 66 per cent of C_2H_5OH, etc.

Schwab discusses the application of the Clausius-Clapeyron equation in the determination of boiling points of organic chemicals. The figures obtained approximate the true boiling points. For details, the original paper should be consulted.

Upright Condensation.—In some chemical and pharmaceutic processes it is found necessary to warm the substance for several hours with alcohol.

To do this in free contact with air is an expensive undertaking, as alcohol evaporates very freely and would therefore pass into the atmosphere and be lost.

To permit economy in alcohol and similar valuable liquids, upright condensation has been devised. This consists (Fig. 96) of arranging the condenser in such relation to the flask that, as the vapors of the alcohol rise and are condensed, they are immediately dropped back into the flask, and by this means it is possible to keep alcohol at the boiling point for weeks at a time without apparent loss.

Two illustrations of upright condensation may be taken from former pharmacopœias. In U.S.P. 1890, spirit of phosphorus was made by heating phosphorus and absolute alcohol in an upright condensing apparatus; while in U.S.P. IX, tincture of cantharides was made by digesting cantharides with alcohol in a tin canister provided with a cork through which a long glass tube was passed.

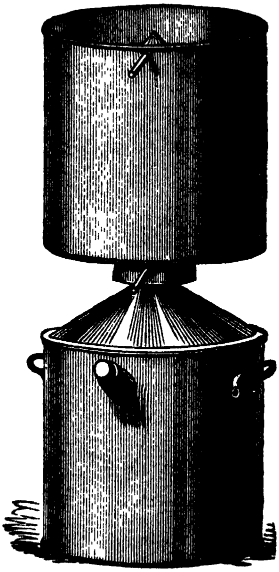


Fig. 94.—Phœnix condenser.

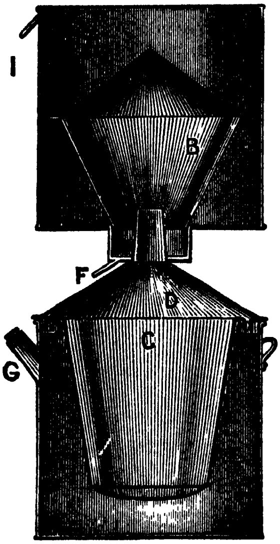


Fig. 95.—Phœnix condenser (outline).

A, Tank for cold water; B, condensing dome; C, boiler; D, connecting dome; E, water bath; F, distilled water outlet; G, bath water outlet; H, steam outlet; I, condensing water outlet.

A compact form of upright condenser is that devised by Soxhlet. This consists of two metallic hemispheres, the inner one communicating with the flask in which the liquid is heated, and the outer one with the water supply; therefore, corresponding to the inner and outer tube of the Liebig condenser respectively (Fig. 97).

Some processes of distillation, as in the extraction of the volatile principles of drugs, are largely performed by intimately mixing the source of the volatile substance with water contained in the boiler, and heating both together, whereby the water and volatile constituents of the drug are volatilized and pass into the condenser, where they are liquefied and separated, the oil usually being immiscible with water.

Such, for example, is the method whereby oil of peppermint is obtained from the herb, and in all such cases of distillation care must be exercised to prevent the herb from coming in direct contact with the bottom of the vessel, the greater heat of which is apt to cause a partial charring of the organic drug, with subsequent decomposition of same, giving rise to the disagreeable tarry odor called "*empyreuma.*" This decomposition is obviated by preventing the drug from resting on the bottom of the boiler, either by suspending the drug in an appropriate cloth, bag, or sack, or by having a still with a wire basket, such as is shown in the picture of the Remington still (p. 123).

Far better is the protection of the drug accomplished in the process of *steam distillation,* which consists in generating the steam in an appropriate tin can provided with safety tube, and passing the steam thus generated into the flask or can containing the drug, and an appropriate quantity of water (Fig. 98).

Through this the steam passes, carrying the volatile constituents of the herb into the condenser, where both become fluid.

Destructive Distillation.—In other pharmaceutic processes the decomposed products of the substances heated are desired. In some cases the substance is placed in a large iron retort and heated strongly, whereby the substance is decomposed and the volatile decomposition products pass over and are condensed by appropriate means. Such condensation is used in the destructive distillation of wood, whereby we obtain the valuable commercial products, wood alcohol, acetone, and acetic acid. (See p. 649.)

Vacuum Distillation.—As mentioned on p. 109, evaporation is facilitated by removing air pressure from vessel where the evaporation occurs, and at that place details for large operations of that character were given. In the chemical laboratory small operations of evaporation and condensation can be readily accomplished in the apparatus shown in Fig. 99, which, it will be seen, consists of two distilling flasks connected by air-tight rubber corks. One of the flasks acts as the boiler, while the other serves as condenser, and to the exit tube of the latter is fitted the outer tubing connecting with the vacuum pump (p. 110).

In the neck of the flask acting as the boiler is fitted a rubber stopper, through the orifice of which passes a glass tube drawn to a capillary point. The outer end of the tube is fitted with a piece of rubber tubing which is opened and closed by means of a pinch cock. The object of this tube is to permit egress of sufficient air to prevent bumping; and if the temperature of the distillation is to be observed, the thermometer is inserted in the tube.

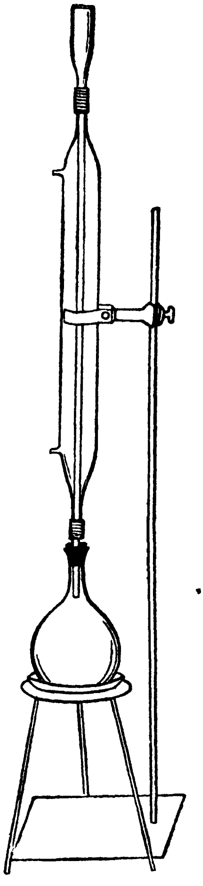


Fig. 96.—Invert condenser.

The condenser is chilled by a steam of running water, while the boiler is heated by means of a Bunsen burner, with or without water bath.

Special Stills.—As mentioned above, the word "still" is usually applied in the technic to a piece of apparatus, made of metal, consisting of boiler and condenser, and the varieties of these special stills are so numerous that space forbids more than mention of a few of the typical forms.

One of the most popular is the old-fashioned still with condensing

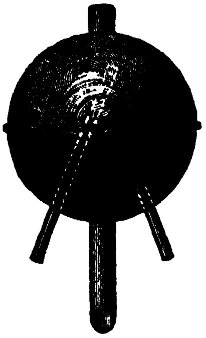


Fig 97.—Soxhlet's invert condenser.

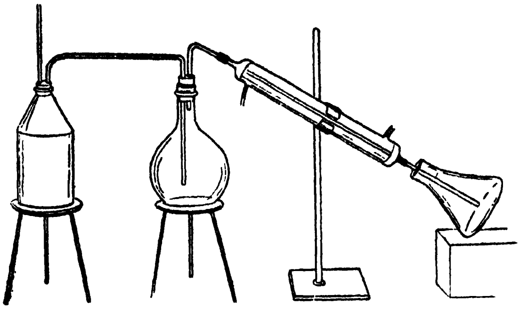


Fig. 98.—Steam distillation.

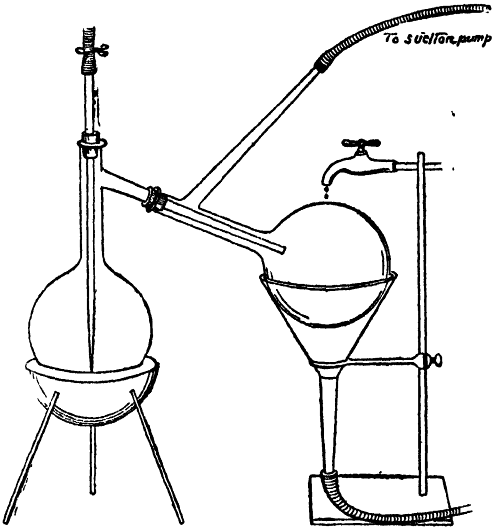


Fig. 99.—Vacuum distillation.

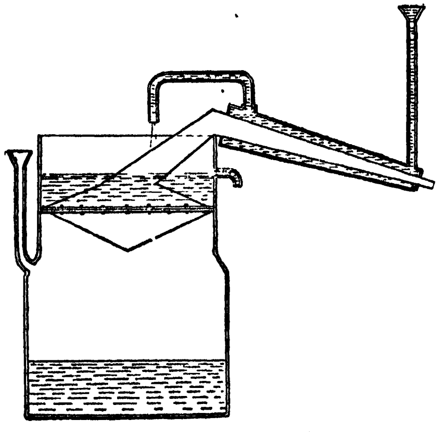


Fig. 100.—Curtman still.

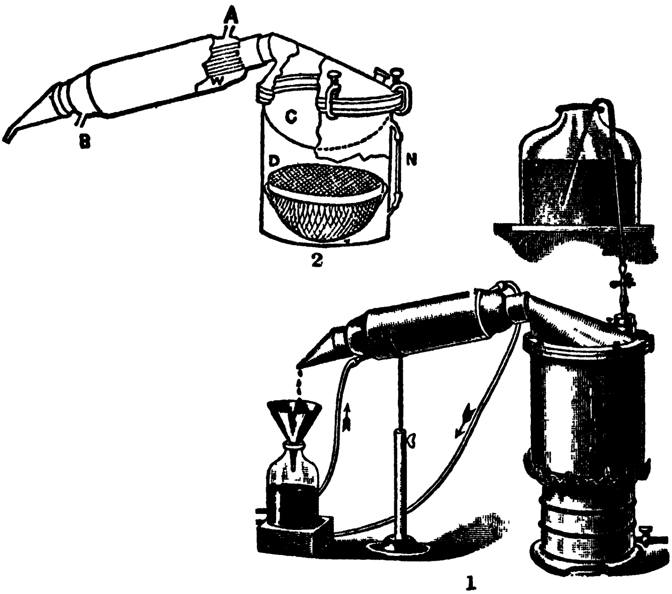


Fig. 101.—The Remington still: 1, Apparatus set up ready for use; 2, section showing condenser and wire basket. A, Condensing water outlet; B, condensing water inlet; C, boiler; D, wire basket; N, water gauge; W, condensing tubes.

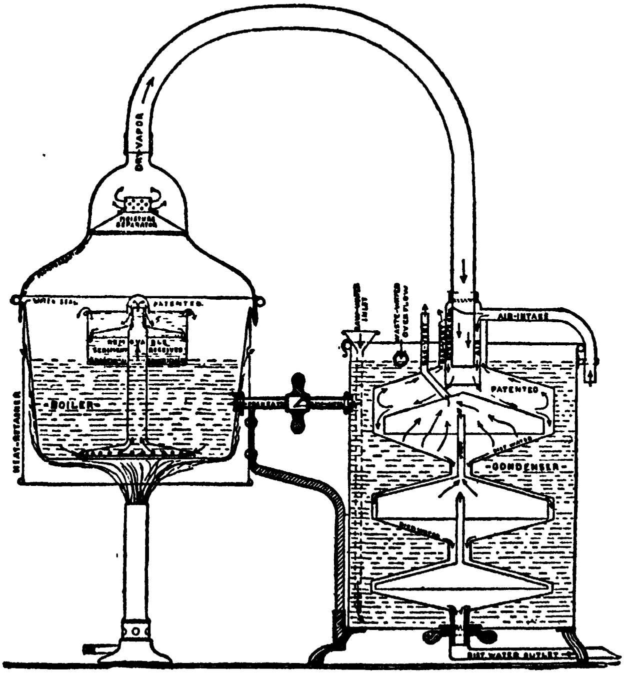


Fig. 102.—Links water still:

worm, and, besides this, mention may be made of *Phœnix pharmaceutic condenser* (Fig. 94), which is of the alembic form; the *Curtman still* (Fig. 100) which is a combination of the alembic and retort form, and the *Remington still,* in which the condenser occurs in a modified form of the Liebig condenser (Fig. 101).

A noteworthy feature in the Remington still is the arrangement of the condenser with 7 parallel tubes placed in the same outer cylinder, on a principle akin to the tubular boiler. This modification gives a very extensive condensing surface in a comparatively compact form (as in a condensing worm), and possesses the advantage over the condensing worm that all tubes are straight, hence can be easily cleaned. This still is provided with a wire basket in which the drug desired to be distilled can be placed, thereby preventing contact with the bottom of the boiler and the consequent empyreuma.

Stokes has devised an automatic wall apparatus that distils ½ gallon of water per hour with the consumption of 10 cubic feet of gas; Link has patented the still shown in Fig. 102; while Sargent has constructed an electric water still distilling 4.5 liters of water per hour with the use of a 110-volt current (Fig. 103).

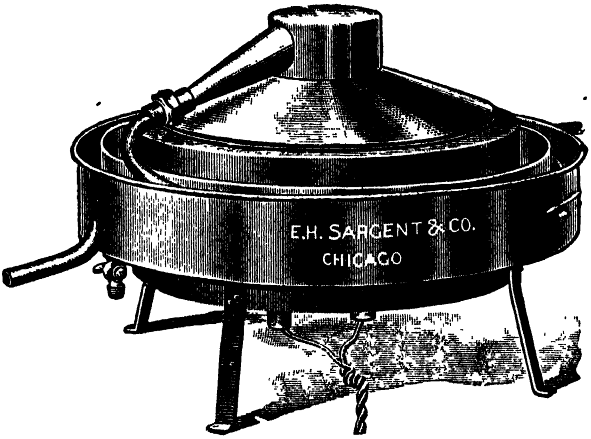


Fig. 103.—The Sargent electric still.

The *Lloyd still* and concentrator works upon the principle that evaporation occurs rationally from the surface of a liquid, and that it is unnecessary to keep the contents of a still or an evaporator heated during the process. If the heat be applied to the surface of a liquid, the menstruum is instantly separated from the dissolved matters, which, dropping down into the still, are immediately cooled, and remain cool until the end of the operation. By automatically conducting a percolate to the heated surface, the distillate being conducted back upon the drug in the percolator, continuous distillation and percolation result. The application of the heat is instantaneous, whether the amount of drug worked be large or small. By this method the most delicate organic structures are preserved in solutions where a prolonged boiling would dissociate and destroy.

Large Scale Distillation.—In the manufacture of acids and of organic solvents distillation plays an important rôle and in few lines of pharmaceutical and chemical manufacturing has more progress been made than in the construction of highly efficient distilling apparatus. A typical rectifying apparatus of this character is pictured on page 656 and for further details the reader is referred to papers mentioned in the Bibliography at the end of this chapter.

SUBLIMATION

This is the process of distilling a solid; of converting the solid into a vapor, and condensing the vapor back to a solid.

We generally term a solid that can be converted into a vapor "a volatile solid," but it is a question whether the latter phrase should not be limited to a solid which volatilizes at ordinary temperatures, such as iodine or camphor. Sulfur can be sublimed if heated to 448° C.; but it can scarcely be considered as a volatile substance.

A comparison of the three stage of the process shows how closely akin is the process to distillation:

Distillation	Liquid-gas-liquid.
Sublimation	Solid-gas-solid.

The object of sublimation, like distillation, is to obtain a volatile drug in a purer form. Sublimation is also one method of obtaining crystals.

As the apparatus employed in distillation was one of two types, so in sublimation the operation is carried on in apparatus of either the alembic or the retort type.

If the vapors are condensed directly over the vaporizing substance, if the condenser is but little cooler than the temperature of vaporization, the sublimate will form in a solid mass—a *cake sublimate*. If, on the other hand, the condensing space is on one side, hence considerably cooler than the vessel in which the substance is vaporized, we get a fine powder —a *powdered sublimate*.

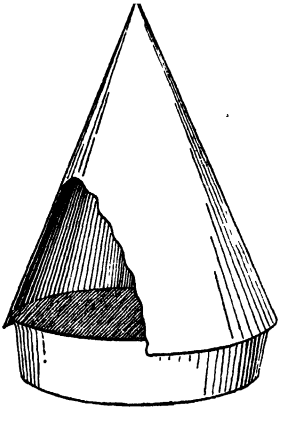


Fig. 104.—Subliming benzoic acid.

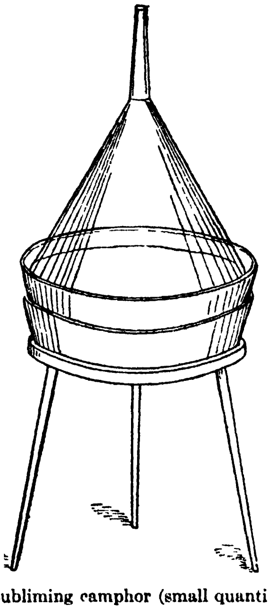


Fig. 105.—Subliming camphor (small quantities).

No artificial means of refrigeration are needed in sublimation, the air being sufficiently cool to condense the vapor into a solid form.

Several of the official sublimed substances can spontaneously change from a solid to a gas, without assuming the intermediate form of a liquid. This can be noticed in any bottle in which camphor has been kept, where handsome crystals, products of spontaneous sublimation, can be found in the upper part of the bottle.

Apparatus.—Since in sublimation the condensation is usually effected at the temperature of the air, the apparatus used in the process is very simple, but similar to distillation in possessing the boiler part and the condensing part.

In small operations the alembic subliming apparatus consists of a dish covered with a cornucopia of paper, or with a glass funnel terminating with a wide-mouthed bottle (Figs. 104 and 105), while when powdered sublimates are desired, an ordinary retort is used as the boiler, and a wide-mouthed bottle as condenser (Fig. 106).

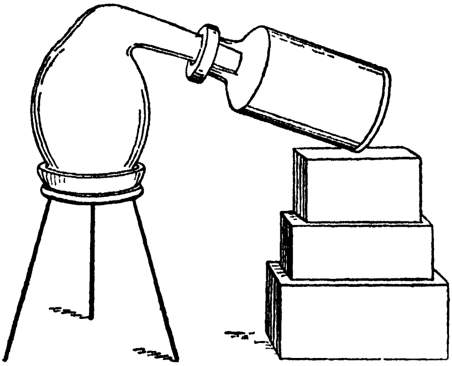


Fig. 106.—Sublimation of sulfur using a glass retort.

In the sublimation of large quantities of chemicals the apparatus is usually of cast iron, the condenser consisting either of the cast-iron dome over the retort, or a well-cooled room into which the neck of the retort projects. Apparatus of the first kind (Fig. 107) is used for the sublimation of such cake sublimates as ammonium chloride; whereas the apparatus of the second kind is used for the sublimation of sulfur and the like, where a powder is desired.

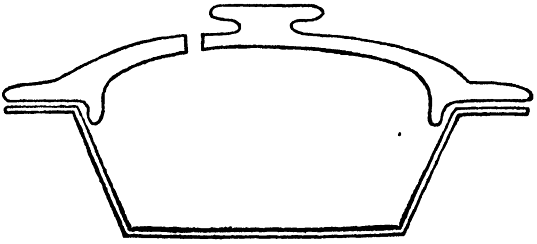


Fig. 107.—Subliming vessel for ammonium chloride.

LABORATORY EXERCISES

SUBLIME BENZOIC ACID

Take benzoin (say, 5 to 10 Gm.), rub with about twice the quantity of sand, and put in tin ointment box. Cover with paper cornucopia, and heat on sand bath not exceeding 120° C. for an hour. Then open paper and note small shining crystals (Fig. 104).

Remarks.—*Sublimation.* (See p. 125.)

For condensing the vapor of solids, cool air is usually sufficient. Avoid high heat, as it causes decomposition, with formation of irritating vapors.

SUBLIME CAMPHOR

Take lump of camphor (5 to 10 Gm.) and put in small evaporating dish. Cover same with small inverted funnel, which should fit inside the dish, and place over neck of same the beaker. Place on water bath and heat. The camphor sublimes, and its vapors condense in funnel and beaker in handsome crystals (Fig. 105).

DESICCATION

Desiccation is a *process of removing water from a substance at moderate temperature,* thus differing from exsiccation, which means removing the water from a substance at high temperatures.

Desiccation is one of the most commonly applied processes in domestic economy. For example, it would be perfectly correct to call the drying of a wet cloth by exposing it to air and sunlight "desiccation."

Objects.—Desiccation is employed to aid in the preservation of the drug; to reduce the bulk of same; and to facilitate comminution.

That the drying of a substance aids its preservation by preventing the formation of mold is a fact well established, it being generally known that when many organic substances are allowed to remain in a permanently moist condition, moldiness and ultimate decomposition result.

It is a fact worthy of the pharmacist's attention, inasmuch as it is a dictum that it is only a damp substance which becomes moldy, and, therefore, mold can be prevented by keeping the substance in a dry place.

Bourquelot has shown that simple desiccation of plants does not wholly prevent deterioration, since drying at ordinary temperatures does not destroy the oxidizing enzymes. (See Chap. LI.) These can be destroyed only by submitting the plant to higher heat and preferably to heated alcohol vapors. This process now largely used in French pharmacy is called "stabilization of drugs."

Another phase of desiccation is the keeping dry of those drugs like ergot which are prone to absorb moisture from the air. The sixth edition of the German Pharmacopœia directs that such drugs be kept in vessels over freshly burnt lime and several types of drug closets and canisters have been devised for this purpose. The U.S.P. XI (pages 6, 7, 154, 169) gives careful directions as to the storage of official vegetable drugs, extracts and fluidextracts. Specific directions for storage are given in many of the monographs on chemicals and particularly in the case of such potent drugs as digitalis, ergot and volatile or readily decomposable drugs.

That desiccation reduces the bulk of a substance can be shown in the drying of fresh herbs. Fresh herbs contain from 70 to 80 per cent moisture, therefore the dry drug will weigh only about one fifth of the fresh drug, and will occupy a much smaller space. The presence of moisture in a fresh drug renders it practically impossible to reduce same to powder, and if attempted by pounding the fresh drug in the mortar, a pulp results; hence it is given as a third object of desiccation that the process facilitates comminution.

Desiccation is not merely the drying of the fresh herbs, but means the removal of moisture from any drug; for example, if a chemical, like potassium acetate, absorbs moisture and becomes liquefied, there is no need of throwing away the liquid mass, since by applying a gentle heat to the substance, the moisture will be eliminated and the dry chemical obtained.

In the same way, in making such pharmaceuticals as pills or lozenges, the freshly finished compound will be moist, and before putting same away, they should be freed from this moisture by desiccation. If such pills or lozenges are put away before completely dry, they will become moldy.

Apparatus used in desiccation is as varied as the different characteristics of the subjects to be desiccated. Thus in drying the herbs no apparatus is needed other than stout gunny bags, which are suspended in places having free access to air. In the smaller desiccations performed in laboratories several forms of apparatus are used. Among these mention may be made of *drying closets* (Figs. 108 and 109), which consist of enclosed shelves having access to a flue and heated either by a steam radiator, gas stove, or electricity. Figure 110 utilizes an electric fan to create the necessary air current. For still smaller operations *drying ovens* are used, these being heated by means of the Bunsen burner, and usually jacketed, so that a water-bath heat may be maintained if desired (Fig. 111). Such ovens can be maintained at a uniform temperature by use of special appliances called *thermostats.*

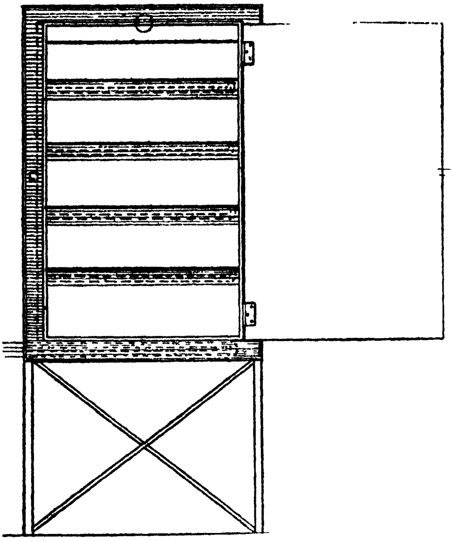


Fig. 108.—Drying closet.

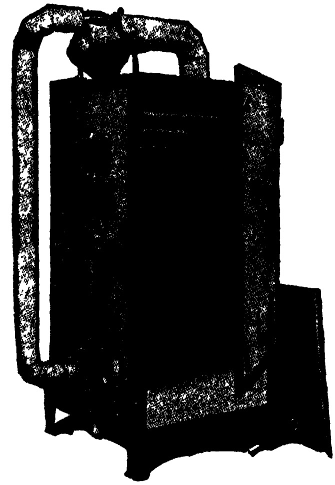


Fig. 109.—Stokes' electric drier.

Drying on a large scale is carried on in rotary driers, vacuum driers and also by passing of the substance on belt conveyers through warm rooms or tunnels. For details, a work on technical chemistry should be consulted.

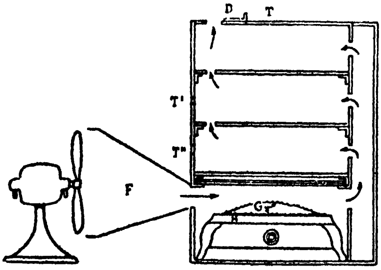


Fig. 110.—Newton and Cook laboratory drier. (Courtesy of "Chemical Abstracts.")

H is a hot plate covered with wire gauze *G*. The fan blows air through funnel *F*. *D* is a damper. Arrows show direction of air current. Thermometers are inserted at *T*, *T'* and *T''*.

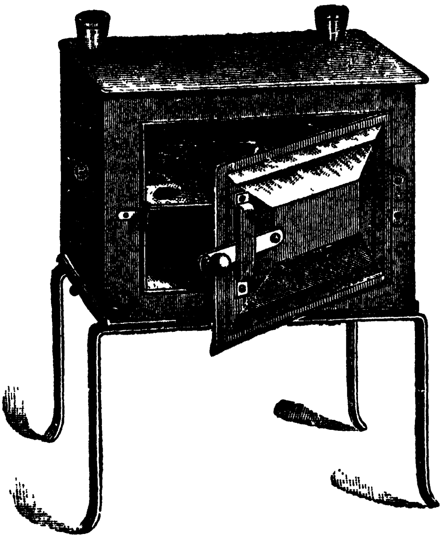


Fig. 111.—Drying oven.

To prevent a substance which has been desiccated from absorbing moisture from the air, recourse is had to *desiccators,* these usually consisting of a glass vessel provided with a ground-glass cover, the joints being made air-tight by tallow or petrolatum, the vessel being so arranged as to contain in an appropriate space sulfuric acid or calcium chloride, both of which substances absorb water with great avidity, thus rendering the air within the container practically water free.

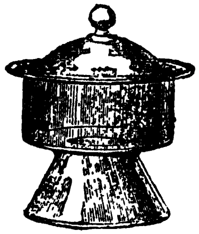


Fig. 112.—Glass desiccator.

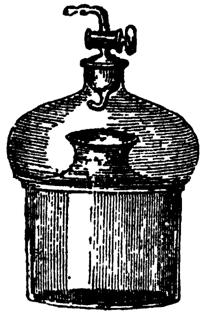


Fig. 113.—Hempel's desiccator.

Of the two forms of desiccators illustrated in Figs. 112 and 113, the Hempel desiccator is arranged to permit a vacuum.

Air Conditioning.—In the large scale production of deliquescent or hygroscopic substances, the quantity of moisture in the work room is at times of vital importance. Engineers have solved this problem and there are now available a number of types of apparatus that will automatically keep the air at a desired degree of humidity.

BIBLIOGRAPHY

Calcination.—Schuster, Ch. Zt., 51, 1927, 666, 708 and 727; Dickie, Jl. Ind. Eng. Ch., 21, 1929, 461.

Crucibles.—(Hessian) Anon., Tonind. Zt., 36, 1912, 1436. (Porcelain and Metal) Blount, Analyst, 43, 1918, 60.

Melting Points.—Menge, A.J.P., 82, 1910, 178; Müller, A.Ph.A., 56, 1908, 52. Bur. Standards Circ. 35, 1918, 1.

Autoclaves.—Wolfe, C.A., 20, 1926, 315.

Latent Heat.—Regnault, through Ganot-Atkinson's Physics, 1910, 379.

Atmospheric Pressure.—Torricelli, through Ganot-Atkinson's Physics, 1910, 151.

Steam Pressure Tables.—Parry, The Steam Engine, p. 322; Wilson, Steam Boilers, p. 303; Ravenscroft, Jl. Ind. Eng. Ch., 21, 1929, 1204.

Boiling Points.—Schwab, Zt. angew. Ch., 43, 1930, 155.

Conditions of Boiling.—Berkeley and Appleby, Proc. Roy. Soc., through C.A., 6, 1912, 442.

Condensation Data.—Hausbrand-Wright, Evaporating, Condensing and Cooling Apparatus, p. 214; Anon., Ph. Jl., 92, 1914, 784; Mourad and Badger, Jl. Ind. Eng. Ch., 22, 1930, 1103.

Evaporation.—(Theory) Thomas and Ferguson, Phil. Mag., through C.A., 12, 1918, 16. (Apparatus) Merrill and Ewing, Jl. Ind. Eng. Ch., 11, 1919, 230; Ure, Jl. Soc. Ch. Ind., 431, 1924, 294; Wester, Arch. d. Pharm., 262, 1924, 575; De Wolf, Jl. Ind. Eng. Ch., 21, 1929, 451; Badger, Jl. Ind. Eng. Ch., 22, 1930, 700; *ibid.*, 20, 1928, 55. (Perevaporation) Kober, Jl. Am. Ch. Soc., 39, 1917, 944 and 40, 1918, 1226.

Distillation.—(History) Lippmann, Zt. angew. Ch., 25, 1912, 1680; Schelenz, *ibid.*, 25, 1912, 2526. (Theory) Gay, Chim. et Ind., through C.A., 14, 1920, 1479; Peters, Robinson, Lewis and others, Jl. Ind. Eng. Ch., 14, 1922, 476 to 492; Winter, Chem. Met. Eng., 30, 1924, 18; Butcher, Ind. Ch., 6, 1930, 199. (Condensers) Speter, Zt. angew. Ch., 21, 1908, 625. (Invert condensers) Meyer, Ch. Zt., 34, 1910, 357; Keyes, Scientif. Month., 28, 1929, 274; Egloff and Lowry, Jl. Ind. Eng. Ch., 21, 1929, 920. (Bumping) Gernhardt, B., 27, 1894, 964; Arny, Pharm. Era, 25, 1901, 700; Pieszckek, Ch. Zt., 36, 1912, 198. (Steam distillation) Bennett, A.Ph.A., 55, 1907, 877; Roff, Ph. Jl., 106, 1921, 28. (Fractional distillation) Noyes, Jl. Am. Ch. Soc., 23, 1901, 463. (Distilling apparatus) Lepinasse, A.Ph.A., 56, 1908, 439; Kremers, Ph. Rev., 14, 1896, 15; Masferrand, Jl Soc. Ch. Ind., 39, 1920, 299T; Rodebush, Jl. Ind. Eng. Ch., 14, 1922, 1036. (Distilling column) Noyes, Jl. Ind. Eng. Ch., 20, 1928, 1190;

Robinson, Jl. Soc. Ch. Ind., 47, 1928, 405; Othmer, Jl. Ind. Eng. Ch., 22, 1930, 322; Pope, Jl. Soc. Ch. Ind., 50, 1931, 318.

Special Stills.—Curtmann, A.J.P., 41, 1869, 197; Remington, A.J.P., 50, 1878, 15; Lloyd, U.S. Pat. 777,115, Dec. 13, 1904; Sargent, Ch. Zt., through A.Ph.A., 56, 1908, 67; Stokes, A.J.P., 83, 1911, 115; Link, Am. Dr., 63, 1915, 339; Anon., Jl. Soc. Ch. Ind., 45, 1926, 297.

Desiccation.—(General) Hausbrand, Z. Ver. dtsch. Ing., through C.A., 16, 1922, 4288. (Loss in drying) Lieurance, A.Ph.A., 41, 1893, 480. (Laboratory Driers) Newton and Cook, C.A., 22, 1928, 4009. (Vacuum drying) Passburg, Jl. Soc. Ch. Ind., 49, 1930, 397. (Desiccating canisters) Hempel, Zt. anal. Ch., 30, 1891, 697; Anon., Ph. Zt., 56, 1911, 218, 304 and 775. (Stabilization of drugs) Bourquelot, Pharm. Era, 45, 1912, 559: Béguin, Ph. Acta Helv., 2, 1927, 196 and 227; *ibid.*, 3, 1928, 117 and 123; Jl. ph. et ch. [8], 12, 1930, 49; Siegfried, Ph. Acta Helv., 3, 1928, 153. (Air conditioning) Fleisher, Jl. Ind. Eng. Ch., 23, 1931, 732.

CHAPTER VI

COMMINUTION

This is the process of reducing a substance to finer particles, and, according to the fineness into which the particles are divided, we subdivide the subject into the topics: cutting, slicing, chopping, rasping, grating, bruising, grinding, pulverizing, and triturating.

To obtain the substance in still finer form than that yielded by trituration, the processes of levigation and elutriation are used.

These several objects will be considered in regular order, with mention of apparatus used in each case.

Objects.—The chief object of comminution is to present the drug in a form in which it is more susceptible to solution. In fact, with the exception of comminution for the purpose of making the so-called "dusting-powders," all processes of comminution used in pharmacy are made with the intention of facilitating solution of the drug or its active principles.

VARIETIES OF COMMINUTION AND APPARATUS USED

Cutting, slicing, and **chopping** are familiar operations, rarely used in pharmacy, except for the preparation of drugs for the more complete processes of comminution. Cutting and slicing can, of course, be performed with any appropriate knife and chopping with any sharp instrument, such as a hatchet or cleaver, and in place of these familiar instruments, the best apparatus in pharmacy for the purpose is the herb-cutter (Fig. 114). This can be used in cutting practically all drugs, and even for vanilla beans, prior to making tincture therefrom. However, for the cutting of vanilla beans, nothing is better than to take about a dozen beans, wind

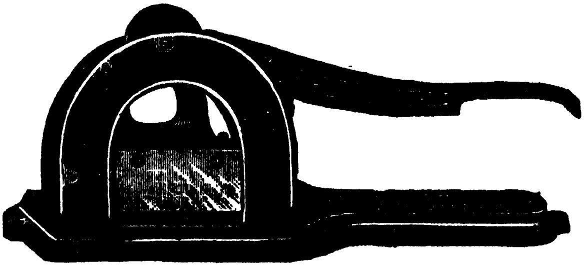


Fig. 114.—Herb cutter.

them tightly with a piece of stout twine, and slice them down with a sharp carving knife. In separating glands for the manufacture of various glandular preparations from surrounding tissues surgical knives are used.

Rasping and **grating** are not used very much in pharmacy, about the only drug which is convenient to rasp being guaiac wood, while grating is limited to the comminution of the small portions of nutmeg or lemon-peel, a nutmeg-grater being an inexpensive and convenient apparatus to have at a prescription counter.

Contusion or **bruising** is performed in a mortar, and for this special purpose the old-fashioned iron mortar is very useful. By means of the instrument almost any drug can be reduced to powder of almost any fineness, but the process is so tedious that it has largely been replaced by grinding in a mill.

Other objections to the iron mortar are that pounding therein is a very noisy process, and a continuance of this pounding in a large mortar is apt to jar the building where the operation is conducted, hence such an apparatus should be used only on a firm foundation, and if on an upper floor, the mortar should be placed on a rafter and, if possible, over a supporting pillar.

Wooden mortars were formerly in considerable use, and at present are sometimes used in the bruising of acid drugs, such as beating up a tamarind pulp preparatory to making confection of senna, while huge marble mortars, which formerly enjoyed considerable popularity, have now almost completely fallen into disuse. Mortars used for contusion, the familiar form of which are seen in appended cut (Fig. 115) must not be confounded with the smaller mortars used in process of trituration at the counter.

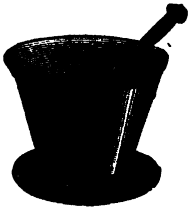


Fig. 115.—Iron mortar.

Grinding and Pulverizing.—Grinding is the process of reducing substances to moderately coarse powders. Pulverization is a term usually applied to grinding to a still finer powder. In both cases the operation is carried on in special apparatus called mills.

A discussion of mills, as of stills, means mention of a vast variety of apparatus adapted for the various requirements of the trade. For example, in a thorough discussion of the subject, mention should be made of flour mills and mills for other large technical processes. Even in the consideration of the strictly pharmaceutic operation of drug grinding, almost as large a number of mills could be discussed, and picking from this array the most typical forms, it is necessary to discuss the following, with only a brief mention of their principle of action, leaving the illustrations to convey the main characteristics.

Buhrstone Mill.—This is the ordinary form of mill, and is made of two stone corrugated plates which rotate on each other. On the rotating surface of the two are made grooves which act on each other, and on the drug interposed, in a manner somewhat similar to the blades of a scissors, clipping the drug to pieces at the same time that the weight of a stone crushes the drug to powder. Such form of mill is seen in Fig. 116.

Roller Mill.—This consists of two large rollers of steel or iron, which revolve on each other and can, by means of suitable mechanism, be made to approach and become remote from each other. Such mill works entirely from the dead weight of the roller, and is used for the powdering of greasy or soft substances.

Chasers consist of two movable rollers rotating on a central axis on a steel base (Fig. 117). Such a chaser mill is used in the making of chocolate paste and the like.

Barrel or *cannon-ball mills* consist of barrels made of oak or steel, containing iron or stone spheres about the size of cannon-balls, the barrel being arranged to rotate upon an axis, and when this is done, the balls roll to and fro with sufficient force to powder the drug contained in the barrel (Fig. 118). The advantage possessed by a barrel-mill is that the process of pulverization is made with but little loss, because none of the dust escapes. Its objection, however, is the loud noise of the rolling cannon-balls.

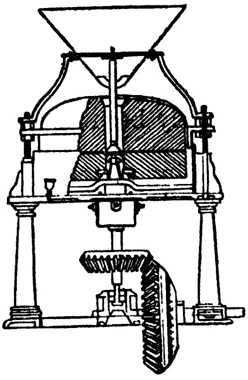


Fig. 116.—Buhrstone mill.

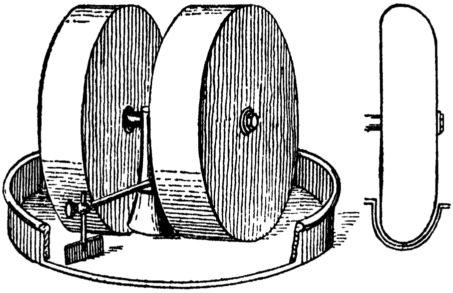


Fig. 117.—Chaser mill.

Mead's disintegrator is the most efficient type of the modern power drug-mill, and can best be understood by studying the cuts (Figs. 119 and 120). As seen therein, it consists of a steel disk having on the outer edges a series of steel projections. This disk rotates in a case the upper edge of which consists of corrugated steel, against which the projections in the disk come almost into contact. The unique principle of the mill is the fact that it performs its work not by reason of its weight, but because of the enormous velocity at which the disk rotates, the drug placed in the mill being thrown up by the disk and its projections against the steel

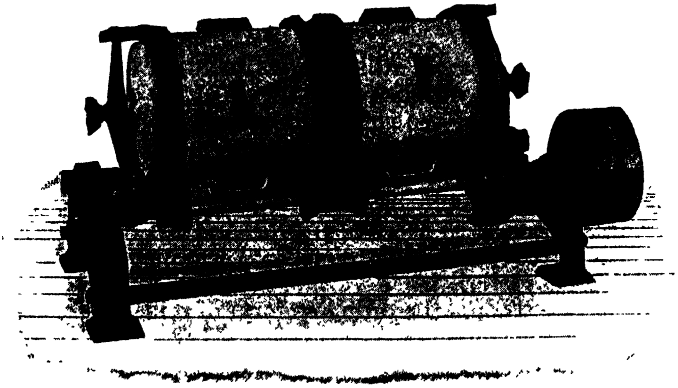


Fig. 118.—Stokes' barrel mill.

corrugations with a force somewhat akin to a cyclone and is so literally torn to shreds. A modern modification of the Mead mill is the Wiley Laboratory Mill (Fig. 121).

All the mills above mentioned operate entirely by steam or electric power, and are, therefore, beyond the province of the retail pharmacy, hence of more importance to pharmacists are the mills now to be discussed.

Hand Power Mills.—Of the many varieties of hand mills, three types can be considered: Those in which the drug is crushed between two vertical grinding surfaces, those in which the grinding surfaces are horizontal, and those in which the grinding surfaces are conic.

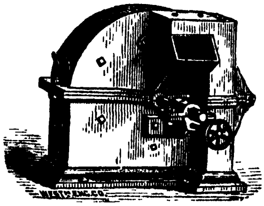


Fig. 119.—Mead disintegrator.

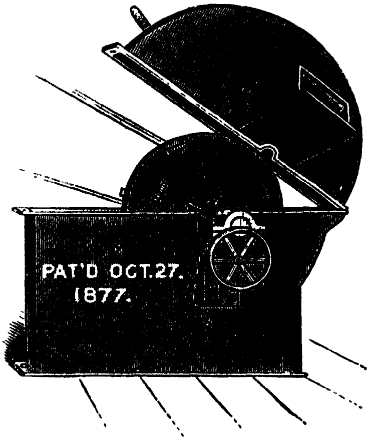


Fig. 120.—Mead disintegrator (open).

An example of the first type is found in the old-style Swift mill; the second type is shown in the Hance mill, and the third type is represented by the Enterprise mill, all of which are shown in the illustrations (Figs. 122, 123, and 124).

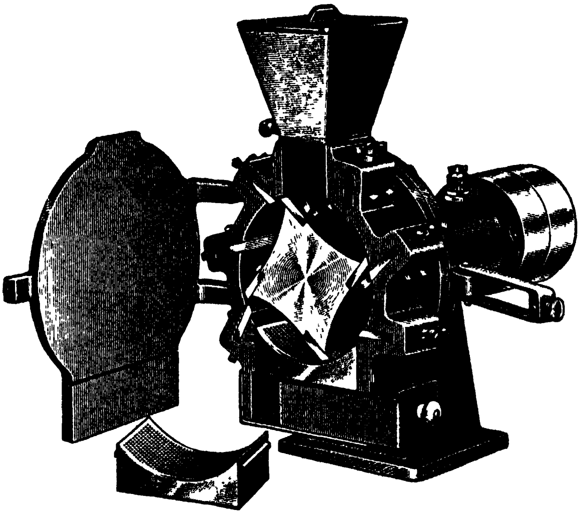


Fig. 121.—Wiley laboratory mill.

Of these mills, the most serviceable is the conic variety, and in selecting a mill it is highly advisable to choose one in which the plates are easily removed for cleaning. By means of a drug mill, a substance can be readily reduced to powder provided suitable care is taken by the operator, it being a good rule to first grind the substance coarsely, then return it to the mill, bringing the plates closer by means of the screws intended for that purpose, grind the drug again, and possibly repeat the operation with the screws still tighter. In rotating the plate by means of the crank or wheel, a uniform and steady motion should be maintained, far better results being obtained by a slow persistent motion than by rapid and spasmodic efforts. Under no circumstances should the mill be worked so rapidly as to overheat the plates. With proper treatment a drug-mill should last a lifetime.

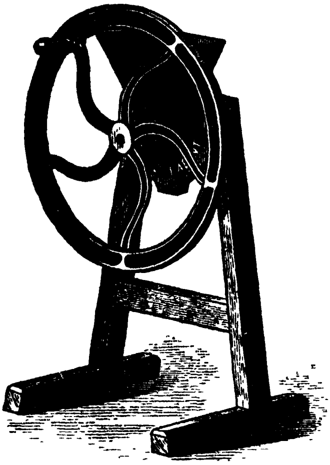


Fig. 122.—Swift mill.

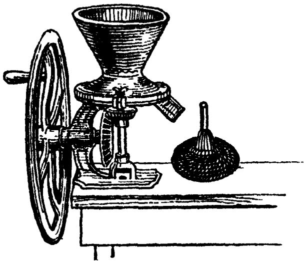


Fig. 123.—Hance mill.

In grinding and sifting irritating and poisonous drugs, such as soap bark, the mouth and nostrils of the operator should be protected by covering them with a moistened towel.

Pebble Mill.—This consists of a large cylinder holding about 55 per cent of the material to be ground and about 45 per cent pebbles. By rotating the cylinder the pebbles fall through the material and break up agglomerations or lumps.

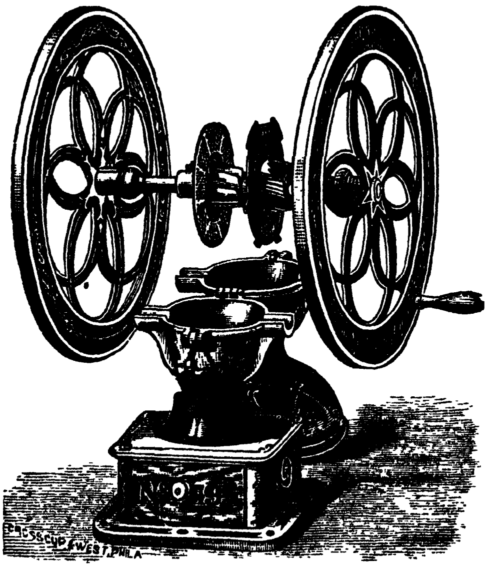


Fig. 124.—Enterprise drug-mill.

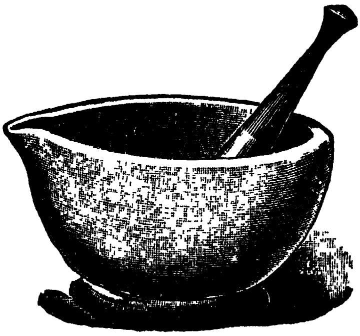


Fig. 125.—Triturating mortar

Colloid mills are now available which are used for finely disintegrating, dispersing, and emulsifying. They are high-speed mills which grind by forcing the material through the minute clearance formed by the swiftly revolving steel "rotor" and the stationary steel "stator." The faces of the "rotor" and "stator" are machined with such precision that they can be adjusted to form an exact clearance of $\frac{1}{2000}$ in. throughout their entire circumference.

Trituration is the process of reducing a substance to a finer powder than is usually obtained by grinding in a mill, and is generally accomplished by placing a drug in a mortar and acting on it by the rotary action of the pestle. The apparatus used in trituration is the pestle and mortar aided by the spatula, and for trituration the pestle and mortar of wedgewood ware should be of the design shown in the appended illustration (Fig. 125), while porcelain mortars and pestles are usually of the shape shown in Fig. 126. For triturating powders which become electrified and hence sticky, like salol, porcelain mortars are preferable to wedgewood. Glass mortars are frequently employed for triturating, while for very hard substances agate mortars are sometimes used.

The pestle accompanying the regulation wedgewood mortar has usually a wooden handle which is put into the wedgewood base in a very crude way, usually by pouring a mixture of rosin and wax into the socket and placing the handle in it while the mixture is still warm. Usually a pestle so fastened is very inconvenient, as the rosin and wax will chip off and fall into the substance being triturated. If it is used in trituration of warm ointments, the wax is apt to soften, and if employed in mixtures containing alcohol, the alcohol is apt to dissolve the rosin.

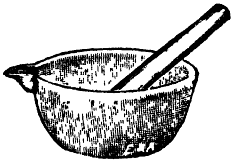


Fig. 126.—Porcelain mortar.

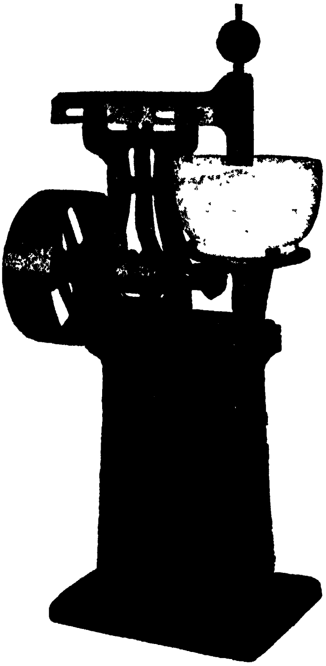


Fig. 127.—Stokes' power mortar.

It is a good rule to fasten the pestle handle securely as soon as purchased, and this is easily done by removing the handle from the base by gentle warmth, cleaning the socket free from the resinous matter, and then pouring into the socket a thin mixture of plaster of paris with water, inserting the handle immediately, and allowing it to stand until the mixture has completely set. A handle so fastened usually remains attached to the base.

As there is, however, some danger of the chipping of the plaster, a cement consisting of glycerin and oxide of lead (litharge) made into a paste has been recommended.

For trituration of large amounts of material power mortars (Fig. 127) are available.

A wedgewood mortar after continual use becomes grimy and cannot be cleaned by the simple application of soap and water. To thoroughly cleanse such mortar, powder a few crystals of potassium dichromate in the same and rub to a thin paste with sufficient concentrated sulfuric acid; smear same over the mortar outside and in. When the paste is washed off, the wedgewood will be found perfectly clean.

Spatulas.—The object of the spatula in trituration is to scrape the triturated powder from the sides of the mortar, and for this purpose a small spatula convenient to carry in the vest pocket is most convenient.

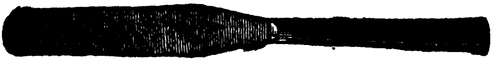


Fig. 128.—Coco-handle spatula.

Of the two forms of spatula shown in illustrations, the nickel-plated form is the most modern and most satisfactory, and every pharmacist should carry one as his personal property (Figs. 128 and 129).

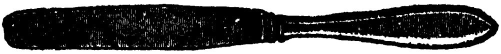


Fig. 129.—Nickel-plated spatula.

Triturations and Triturates.—Aside from the general term, trituration, as applied to reducing drugs to fine powder, a class of preparations called "triturations" have been introduced. These are of homeopathic origin and consist of one part of the medicine intimately mixed with varying parts of sugar of milk, depending upon the strength desired. The Pharmacopœia recognizes triturations containing 10 per cent of the active ingredient rubbed up with 90 per cent sugar of milk. (See U.S.P. XI, p. 413.) Triturates in the form of tablets of various strengths are also made available. They are molded tablets (not compressed) with a sugar of milk base and varying strengths of active ingredients. They are used to a great extent in dispensing potent drugs such as strychnine, atropine, arsenic, and others in prescriptions, thus obviating the necessity of weighing out minute quantities of such drugs.

Sifting is the process of separating finer portions of comminuted drugs from the coarser particles by use of a sieve.

The grinding of a drug, no matter how carefully carried out, will not in itself produce an absolutely uniform powder, the more easily pulverulent portions of the drug being ground more finely than the denser portions. In order to insure a uniform powder, therefore, it is necessary to sift it through sieves, which consist of meshwork either of horsehair or metal wire stretched around a suitable holder (Fig. 130).

The sieve can be made with meshes of equal size, and for sifting drugs, sieves with twenty, thirty, forty, sixty, and eighty meshes to a linear inch are usually employed, the finished sieve being accordingly numbered 20, 30, 40, 60, 80 and 120 respectively.

The best sieves are made with strands of monel metal (p. 594) and some are made as fine as 250 mesh. The standardizing of a sieve is not as simple a matter as it appears at first glance, for the problem involves not merely the number of meshes per linear inch but of far greater importance is the question of the diameter of the wires from which the sieve cloth is made; for upon this factor depends the size of the orifices of the sieve. The Bureau of Standards (see Bibliography) has given the subject careful study and has set standards for the wire used in sieves.

In Germany and other countries of Europe the numbering of the sieve is different from the English and American, it being based on the number of meshes to the centimeter. As an inch is equal to 2.5 cm., the conversion of the German number to the American is not difficult, each unit of the German sieve being equal to 2.5 units of the American sieve. Thus a No. 15 German is equal to a No. 40 American (exactly 37+): while a No. 20 German equals a No. 50 American.

In using a sieve, the ground drug is thrown therein and the particles permitted to fall through the meshes by gently tapping the sieve with a spatula handle or the knuckle, particular emphasis being laid by pharmaceutic writers against forcing the powder through the sieve by rubbing with the hand. It is imperative that all portions of the same drug should be reduced to a uniform powder, hence we should not merely use the first portion that passes through, leaving the coarser particles for a subsequent grinding, but we should take a certain quantity of the drug, grind it with the mill, and sift, repeating the operation until the entire quantity has been passed through, except possibly a small amount of fibrous débris. When all the drug has thus been passed through the sieve, the powder is thoroughly mixed with the spatula, and only then can we say that we have completely powdered the entire drug.

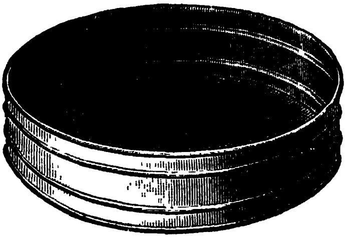


Fig. 130.—Brass sieve.

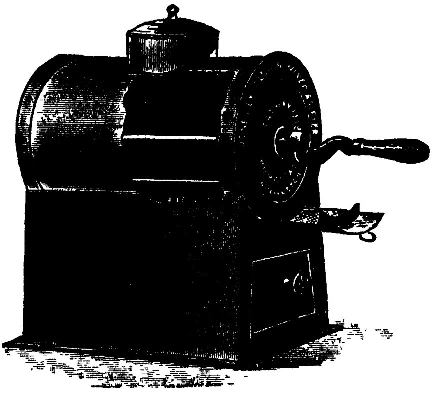


Fig. 131.—Excelsior mixer and sifter.

Powdered drugs are given the same number as the sieve through which all of the particles pass; thus a No. 20 powder means a drug passed through a No. 20 sieve of the requirements set by the Bureau of Standards. However, as much as 40 per cent of the powder may pass through a No. 60 sieve. It will be noticed that in U.S.P. XI powders are not designated by the number of the sieve used, but are mentioned as coarse, fine, etc. A general statement as to fineness of powders is however made in U.S.P. XI (p. 461) from which we learn:

For vegetable or animal drugs—
- A coarse powder is a No. 20 powder
- A moderately coarse powder is a No. 40 powder
- A fine powder is a No. 60 powder
- A very fine powder is a No. 80 powder

For chemicals—
- A coarse powder is a No. 20 powder
- A moderately coarse powder is a No. 40 powder
- A fine powder is a No. 80 powder
- A very fine powder is a No. 120 powder

For extremely fine powders, we use bolting cloth which consists of a cloth with exact meshes made of silk thread. The finer grades of flour are sifted through bolting cloth.

When considerable material is to be sifted the use of a special mixing appliance operated either by hand or other power is advisable, one of the best varieties of such an apparatus being the Excelsior mixer and sifter (Fig. 131).

In large scale chemical manufacturing there have recently been introduced a large number of devices for sifting and mixing powders and for stirring large quantities of liquids. For details as to these the reader is referred to books on chemical engineering.

Dusting powders can be mixed and sifted by pouring them into a bag made of bolting cloth fitted into the neck of half-gallon salt-mouth bottle. The stopper is then placed into the bottle and after shaking the sifted powder will be found at the bottom of the jar.

Levigation is the process of reducing a powder to still finer particles than can be attained through trituration, and is accomplished by placing a substance on an appropriate slab, moistening with a few drops of alcohol, and smearing same over the slab by means of an instrument known as the muller (Figs. 132 and 133). As shown in the illustration, the correct way of using the muller is by rotating it in a circular motion, as if drawing the figure 8. If the slab and muller are composed of porphyry, the process is called *porphyrization*.

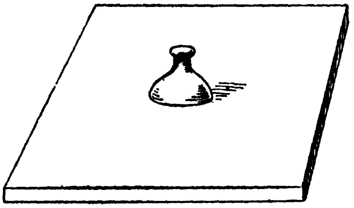


Fig. 132.—Slab and muller.

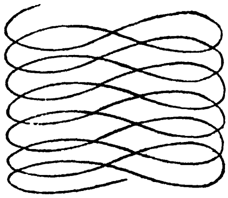


Fig. 133.—Movement of muller.

Elutriation is a crude process of separating coarser from finer particles by suspension in water, hence it is sometimes called "water sifting." It is used only in separating insoluble substances, and is limited to a few cases, such as the separation of chalk from the grit with which it is associated when mined. The freshly mined chalk is coarsely ground, mixed with water to a thin paste, and then thrown into a tank containing water, with the result that the gritty quartz will be washed out and subside, while the less heavy chalk remains for a time suspended in the liquid. After a few minutes the liquid is drawn from the tank into another through a faucet, placed some distance above the bottom of the vessel, and there is allowed to stand until the suspended chalk has separated, whereupon the clear liquid is drawn off and the pasty chalk is obtained almost free from grit. In commerce this chalk paste is usually marketed in the form of cones, and these are produced by the process known as trochiscation.

Trochiscation.—By placing the paste in a wooden vessel shaped like a funnel, and by giving the apparatus sharp raps, the paste drops upon a porous surface, such as a slab of chalk or of earthenware, where it dries in cones, an expert workman being able to make practically all the cones the same size.

Pulverization by Intervention.—There are some substances which are almost impossible to reduce to powder by trituration or other methods of comminution already discussed. Among these the best known example is camphor, which, when pounded with a pestle, becomes a pliable mass. If, however, to the camphor a few drops of alcohol or chloroform be added, it can be powdered without difficulty. This method of reducing a substance to powder by means of another substance is called pulverization by intervention. Camphor powdered with alcohol is apt to cake on standing and this can be obviated by adding to it a minute quantity of colorless petrolatum.

Other examples of pulverization by intervention are the powdering of gold-foil by trituration with potassium sulfate, the potassium sulfate being removed after trituration by treatment of the powder with water. Tin can be powdered by pouring the molten metal into prepared chalk and shaking until thoroughly cold, the prepared chalk being separated from the powdered tin by treatment with diluted acids. Phosphorus can be powdered by simply melting it in solution of salt and shaking the solution until cold.

BIBLIOGRAPHY

Mills.—Redwood, A.J.P., 21, 1849, 19; Blair, A.Ph.A., 23, 1875, 575; Procter, A.J.P., 18, 1847, 255; Ure, Jl. Soc. Ch. Ind., 43, 1924, 1144 and 44, 1925, 321, 349 and 551; Wiley, Jl. Ind. Eng. Ch., 18, 1925, 304; England, A.J.P., 103, 1931, 389.

Trituration.—Minton, Bull. Pharm., 23, 1909, 472.

Power Mortar.—Schultz and Banham, C.A., 24, 1930, 3928.

Pestile Cement.—Vialle, Am. Dr., 19, 1890, 116; Merwin, Jl. Ind. Eng. Chem., 9, 1917, 390.

Spatulas.—McCartney, Am. Dr., 86, Nov., 1932, 58.

Sieves and Sifting.—Remington, Am. Dr., 43, 1903, 199; Hopp, A.Ph.A., 51, 1903, 435; Campbell, Jl. Ind. Eng. Ch., 11, 1919, 761; Anon., Bureau of Standards Circ. Letter L.C., 74, April 15, 1924; Ellington, Jl. Soc. Ch. Ind., 45, 1926, 128T.

Elutriation.—England, A.J.P., 58, 1886, 77.

Pulverization by Intervention.—England, A.J.P., 59, 1887, 598; Anon., N.R., 11, 1882, 112.

Stirring Apparatus.—Belani, Ch. Zt., 50, 1926, 337.

CHAPTER VII

SOLUTION, LOTION, DECANTATION, COLATION, AND FILTRATION

SOLUTION

At various times in the history of pharmacy, definitions of the term "solution" have been set forth which can hardly be considered modern views of the subject. Illustrated by examples, this important topic is not difficult to understand.

When a small amount of common salt is shaken up with water the salt quickly disappears and a perfectly homogeneous liquid is obtained, which has a salty taste, but in which no particles of salt can be detected, even under the highest power microscope. Even on long standing the salt does not settle out of the water, nor can the salt be removed by filtration of the solution. However, on evaporating off the water, the salt is left behind in its original form. If, on the other hand, a little chalk is shaken up with water, a milky mixture is obtained in which the particles can be readily seen and can be separated from the water by settling or by filtration.

In the first case, the salt is taken up or dissolved by the water forming a true solution; in the latter case, the chalk is merely suspended in the water. Between the limits of *true solution* and *suspension* lies the region of *colloid solution* which is discussed on p. 408.

A *solution* may be defined as a homogeneous mixture of two or more substances, which (mixture) can vary in composition continuously within certain limits. The latter part of this definition serves to distinguish solutions from chemical compounds. The latter are of definite and invariable composition, whereas the composition of a solution of salt in water may vary within wide limits.

Physical chemists now divide solutions into three classes: (*a*) *molecular*, such as dissolving sugar in water; (*b*) *ionic*, such as dissolving sodium chloride in water; and (*c*) *colloidal*, such as dissolving gelatin in water.

Again, there are several classes of solutions, arranged according to the physical states of their components. We may have a gas dissolved in a gas, in a liquid or in a solid. We may have a liquid dissolved in a liquid, in a gas or in a solid. We may have a solid dissolved in a solid, in a gas or in a liquid. In pharmacy however, we are chiefly concerned with solutions of gases, liquids and solids in liquids.

That part of a solution which is present in largest proportion is usually called the *solvent*, and the substance taken up by the solvent is termed the *dissolved substance* or *solute.*

When some substances, principally acids, bases and salts, are dissolved in water, their molecules undergo subdivision into particles called "ions." All substances do not ionize and all liquids are not as good ionizing agents as is water.

As to "*ions*" more will be said in Part III.

Solvent.—In order to dissolve a substance a solvent is required, and the character of different solvents varies greatly, investigation showing that many physical combinations, such as the making of solders, fusing of alloys, and the like, follow the same rules as does ordinary solution. Thus, at present, alloys, such, for example, as brass, are considered solutions of the metals of which they are composed.

Pharmaceutically, however, by a solvent is meant a liquid in which the substance is made to disappear and lose its identity.

Of the solvents used in pharmacy, *water* is preëminently the most valuable, as in it dissolve most inorganic chemicals, and such organics as sugars, gums, and glucosides.

Alcohol dissolves resinous drugs, volatile oils, many organic chemicals, etc.

Glycerin is an excellent solvent, dissolving the water-soluble substances and in larger quantities, but its stickiness precludes its general use. Holm and also Birza have reported the solubility of a number of substances in glycerin (see Bibliography).

Acids are used as solvents in some cases, although usually the acid effects a chemical change in the nature of the dissolved substance.

Alkalis are valuable solvents for some substances, as albuminous matter, waxes, starches, and resins, but they, like the acids, usually cause chemical changes in the dissolved substances.

Chloroform and *ether* and *petroleum ether* (or *purified petroleum benzin,* U.S.P.) are solvents for resins, oils, and fats, although their use is somewhat limited.

Carbon disulfide is used for dissolving rubber, while for solution of gutta-percha, chloroform answers.

Of late, in chemical work and in manufacturing industries a large number of organic substances are used as solvents either replacing or in combination with grain alcohol. Among these may be cited *wood alcohol* (methyl alcohol or methanol), *acetone, acetic ether,* "*banana oil*" and the various chlorides of ethane.

Special reference should be made of the large number of organic solvents now used in the manufacture of nitrocellulose and acetyl cellulose lacquers and varnishes. These include chloro derivatives of the hydrocarbons, esters of amyl and other alcohols, etc. For details, see Durran's book on solvents listed on page 15.

Solubility.—By this term is meant how much of a substance dissolves in a given solvent. This can be expressed as (*a*) the number of cubic centimeters of solvent in which 1 Gm. of the substance dissolves (the method of U.S.P. XI); (*b*) in parts by weight of the solvent used to dissolve 1 part of the substance; (*c*) by stating how many parts of the substance will dissolve in 100 parts of the solvent. The range of solubility is practically limitless, some substances in much less than their own weight of the solvent, whereas other substances require many times the weight of the solvent. Thus, silver bromide requires one to two million times its weight of water for solution, while potassium iodide dissolves in seven tenths its own weight of water. When a substance is so slightly soluble as silver bromide, we usually term it insoluble, although practically every substance is soluble to some extent even though it may be only in minute amounts, as in the case of the chemical just mentioned.

To memorize the individual solubilities of all the officials is practically impossible, although the student should know in a general way whether a body dissolves in water or is insoluble, and, moreover, he should be acquainted with the approximate solubilities of such well-known chemicals as potassium bromide, potassium iodide, and potassium chlorate.

Regarding general solubilities in water, the following information relative to inorganic salts is useful, especially in considering prescriptions.

SOLUBLE	INSOLUBLE
All acetates.	Carbonates except those of the alkalis.
All nitrates.	Phosphates, except those of the alkalis.
Sulfates, except barium, strontium, lead, silver.	
All sodium salts.	
Potassium salts, except bitartrate.	
Chlorides, except silver and mercurous.	

This table is of barest outline, and refers only to well-known medicinal substances. For instance, there are a few insoluble sodium salts, but they are not worth consideration in pharmacy. Then remember that the term "soluble" is purely relative. One Gm. of potassium iodide is soluble in 0.7 cc. of water at 25° C., calcium sulfate, on the other hand, requires 410 parts of water at 15° C. to dissolve it; yet both are classed as "soluble" in the above table. Then in the table many substances are missing. For instance, no specific mention is made of copper and zinc salts, or of the silicates, or of a host of other bodies. These omissions are due to the fact that no classification of the substances as to the solubility can be made. Some zinc salts are soluble, some are insoluble; hence they are omitted. Saturated solutions and supersaturated solutions are discussed on pages 144 and 145.

In the present Pharmacopœia (p. 465) is found a monograph on solubility determinations and in it is found the following table of approximate solubilities:

Very soluble	in less than 1 part of solvent
Freely soluble	in 1 to 10 parts of solvent
Soluble	in 10 to 30 parts of solvent
Sparingly soluble	in 30 to 100 parts of solvent
Slightly soluble	in 100 to 1000 parts of solvent
Very slightly soluble	in 1000 to 10,000 parts of solvent
Practically insoluble	in more than 10,000 parts of solvent

Simple and Chemical Solutions.—Due to the investigations of Arrhenius and Ostwald, the former popular distinction between simple and chemical solutions has become obsolete, Arrhenius showing when the chemical dissolves in water, it dissociates into two or more portions, called "ions," and in approximately the same way as some substances separate when under the influence of electricity. In the old method of reasoning a solution of Glauber salt, Na_2SO_4, in water was a simple solution, but if the same salt solution was produced by mixing a solution of sodium hydroxide with diluted sulfuric acid, because a chemical action occurred during the process of solution, this latter solution of sodium sulfate was a chemical solution.

The modern view is that both solutions are identical, consisting as they do of ions of sodium and ions of the SO_4 group; hence in the modern discussion of solution the terms "simple" and "chemical" are eliminated.

Jones' "solvate theory of solutions" supplements the ionic theory by pointing out that in solutions the ions and some of the molecules combine with more or less of the solvent. This idea is now generally known as the "hydrate theory" and the modern conception is a combination of the ionic theory and the hydrate theory; the ions being considered as "hydrated" or associated with molecules of the solvent. Thus Werner expresses the ionization of hydrogen chloride by the following equation:

$$ClH + OHH = ClH.OHH = ClH.OH + H^+$$

while Washburn writes the equation as follows:

$$HCl + (H_2O)_a = (H(H_2O)_b)^+ + (Cl(H_2O)_c)^-$$
$$[a = b + c]$$

Flint in a recent thoughtful paper goes still farther and from generally accepted experimental data postulates the exact number of water molecules attached to the ions of the first 22 elements of the periodic series (p. 406).

In the pharmaceutic discussion of the solutions of the United States Pharmacopœia it is convenient to classify them into those made by simply dissolving the solution in water, which solutions are called "galenics," and those in the manufacture of which by the pharmacist a chemical change occurs. In this sense the term "simple" and "chemical" solutions are still applied, without, however, any intention to intimate that any marked difference exists between the same compound made by simple solution and that made by chemical action.

Conditions of Solution.—In order to facilitate solution it is advisable to pulverize the substance which is to be dissolved, the *advantages of pulverization* being best illustrated by a homely simile.

Imagine a closed book of 500 pages as a lump or crystal of matter. Imagine this exposed to the action of a solvent. This solvent can only attack front, back, and four edges—a surface scarcely equal to that of three leaves. Now imagine that book taken all apart, and its 500 pages spread flat on the floor, and see what an enormous increase in surface. In the same way a great increase is produced in the surface exposed to the action of a solvent when a crystal is reduced to powder.

It is assumed that in most cases, pulverization merely hastens solution without increasing the actual solubility of the particular substance in the particular solvent. Bancroft, however, states that when copper sulfate is reduced to an extremely fine powder (the particles smaller than 0.004 mm. in diameter) its solubility in water is increased 20 per cent.

After powdering the substance and mixing it with the solvent, solution can be facilitated by *agitating* the mixture of the substance and the solvent, and this, because, when we suggest that a solution is a minute subdivision of the substance affecting the very molecules which permeate the molecules of the solvent, it is plain to be seen that in order completely to mix these molecules, agitation is necessary just as some form of agitation aids in the mixing of solids.

Among the conditions of solution the *character of the solvent* has considerable influence, and it is, of course, self-evident that it is useless to attempt a solution of a substance in a solvent which does not affect it. In the same way care must be had in mixing solutions not to add to the liquid another liquid which is apt to precipitate the dissolved substance, even though that liquid is freely miscible with the solvent that has been employed. Thus, alcohol and water dissolve in each other, but if in the water is dissolved a substance which will not dissolve in alcohol, such, for example, as gum arabic, the addition of more than traces of alcohol will result in the precipitation of the gum from the solution.

In the same way, if we have an alcoholic solution of a resinous substance and add water to it, the water will mix with the alcohol, but in the process of solution of the two fluids the resin, which is insoluble in water, is precipitated.

Temperature is a decided factor in influencing solution. Usually a high degree of heat facilitates solution, although not in a definite ratio. Thus 1 Gm. of potassium chlorate will dissolve in 16.5 cc. of water at 25° C., while 1 Gm. of the same salt will dissolve in 1.8 cc. of water at 100° C. This is not always true, however, some substances, notably calcium compounds, being more soluble in cold water than in hot.

Thus 1 Gm. of lime will dissolve in 840 cc. water at 25° C., while it takes 1740 cc. of water at 100° C. to dissolve the same quantity.

An interesting case of temperature variation in solution is found in sodium sulfate (p. 492).

Heat aids solution in rendering molecular subdivisions easier. A body, in fusing, changes from a solid to a liquid, simply because the heat changes the condition of the molecules from fixed rigidity to the mobility characteristic of liquids. This is supposed to be caused by the influence of heat in lessening the cohesive force of the molecules of the substance—by pushing the molecules farther apart. In the case of solution, the molecules of dissolving substance becoming separated by diffusion among the molecules of the solvent, the separation—the pushing apart of the molecules—is greatly facilitated by the application of heat, and that its aid in overcoming cohesion is usually enlisted in solution is shown by the fact that, when a substance is dissolved at normal temperatures, it usually takes up so much heat away from the solvent that the liquid becomes cold. This is especially to be noticed dissolving potassium iodide in water, and freezing mixtures are usually devised on this principle. However, bear in mind that all solids do not chill the solvent on dissolving. For instance, when calcium chloride is dissolved in water, the temperature of the solution is raised considerably. This, however, is supposed to be due to a chemical combination with water, as is also assumed to be the case when sulfuric acid or alcohol is mixed with water. It is interesting to note that while potassium iodide dissolves in water with a distinct lowering of temperature of the fluid, sodium iodide dissolves in water with little or no chilling of the fluid.

Method of Solution.—The ordinary method of dissolving a substance is, as suggested just above, by reducing the substance to a comparatively fine powder in a mortar, then adding the solvent, and triturating until solution is accomplished, and finally filtering the finished solution by passing through a pledget of cotton placed in an appropriately sized funnel. The careful pharmacist, in preparing solutions on prescriptions, should always observe this rule of filtration as the chemicals used are likely to contain minute traces of insoluble impurities, such as fragments of cork from the container, or possibly traces of soot, and to dispense a solution any way other than absolutely clear does not enhance a pharmacist's reputation. In a case of a very soluble salt, such as potassium iodide, the powdering and subsequent trituration in the mortar are not necessary, in such case the solution being quickly effected by transferring the crystals into a flask or the container designed to hold the finished prescription, adding the water, and shaking until solution results. In all such cases the rule of filtration through cotton should be rigidly adhered to, it being a simple matter to pour the liquid from the flask into a graduate and then filter into the bottle.

Percentage Solutions.—The method of calculating the quantity of a chemical required in making a solution of a certain percentage strength is discussed on p. 79. Reference should be made however to papers by Bradley and by Burt in which it is shown that weight-volume solutions are distinctly inaccurate when they are stronger than 5 per cent. For many years the question of what constitutes an accurately prepared percentage solution has agitated the pharmacal profession. "Weight to weight" or "weight to volume" or "volume to volume" may be correct or incorrect according to what is in the mind of the prescriber who writes for a solution of a given percentage strength. The U.S.P. XI has settled the matter as far as official sanction of one or the other method is concerned by the following statement under the heading of "Percentage Solutions":

> In connection with solutions, per cent or percentage has different meanings under different circumstances as follows:
>
> Per cent or percentage, "weight in weight" (*w/w*) expresses the number of grams of an active ingredient in 100 Gm. of the solution.
>
> Per cent or percentage, "weight in volume" (*w/v*) expresses the number of grams of an active ingredient in 100 cc. of the solution.
>
> Per cent or percentage, "volume in volume" (*v/v*) expresses the number of cubic centimeters of an active ingredient in 100 cc. of the solution.
>
> In the dispensing of prescriptions, slight changes in volume due to variations in room temperature and the trifling difference between the volumes of the cubic centimeter and the milliliter are negligible and may be disregarded. When the expression "per cent" is used in prescriptions without qualification, it is to be interpreted to mean: for solutions of solids in liquids, per cent, weight in volume; for solutions of liquids in liquids, per cent, volume in volume; and for solutions of gases in liquids, per cent, weight in volume. For example, a 1 per cent solution is prepared by dissolving 1 Gm. of a solid or 1 cc. of a liquid in sufficient of the solvent to make 100 cc. of the solution. A solution of the same strength may be prepared by apothecaries weight and measure by dissolving 4.5 grains (more accurately 4.5457 grains, at 25° C.) of a solid or 4.8 minims of a liquid in sufficient of the solvent to make 1 fluidounce of the solution.

Circulatory Solution.—Some substances, such as gum arabic and sugar, dissolve comparatively slowly, and in such cases recourse is had to that method of solution known as circulatory solution. In this process the substance is tied in a piece of cloth and suspended just below the surface of the solvent. The liquid in contact with the drug becomes impregnated with the substance, and, being of greater density than the water, sinks to the bottom of the container, giving place to a fresh supply of water, which in turn becomes denser and sinks. In this way a constant downward current of dissolved substance and an upward stream of displaced water produces a circulatory motion of the liquid in the container, hence the name, "circulatory solution."

Saturated solution is one which contains all of a certain substance that the solvent will hold in a solution, and the quantity of a drug in such a saturated solution is, of course, dependent on the relative solubility of the drug. Thus, a solution of lime containing in 100 Gm. only 16 Cg. of calcium hydroxide is a saturated solution, even as is a solution of potassium iodide, 100 Gm. of which contain about 56 Gm. of potassium iodide. In other words, the term "saturated" means the limit of solubility rather than the comparative denseness of solution. An interesting point connected with saturated solution is that a saturated solution of one substance may act as a solvent of another; in other words, in a saturated solution, the solvent powers of that liquid are exhausted only as far as that one substance is concerned, but can be exerted in effecting solution of another substance. Thus a saturated solution of potassium iodide not merely dissolves iodine, but also much more of that chemical than will water alone. In the same way a saturated solution of potassium nitrate will freely dissolve copper sulfate, and this scheme has been used for removing copper impurities from large quantities of potassium nitrate.

Supersaturated Solution.—Under certain conditions, a solvent sometimes takes up and holds more of a salt than is indicated by the solubility of that salt.

This is particularly the case when the salt is treated with water of a temperature higher than normal. As already mentioned, hot water will usually dissolve more of a salt than will cold water, and such solution, on standing, usually deposits the amount of salt in excess of the quantity soluble at ordinary temperatures.

A solution of this kind, holding more of the salt than is normally dissolved, is said to be a supersaturated solution, and in some cases such a supersaturated solution will remain fluid without depositing the excess until violently agitated. A striking illustration of this is shown in the case of sodium sulfate (p. 492).

Colloidal solutions are now extensively used in pharmacy. These are discussed on p. 408.

Volume Changes in Solution.—In effecting solution between a certain volume of a chemical and a certain volume of its solvent, the resulting solution usually occupies less space than do the two ingredients. In other words, contraction of volume occurs in effecting solution. By this, of course, reference is not made to the fact of the solvent occupying the interstices or air spaces found in a certain volume of a crude chemical, but what is meant is the actual volume of the solvent itself independent of air spaces. Thus sugar (specific gravity, 1.336) has a specific volume of 0.748, and 85 Gm. of sugar, therefore, would occupy the space of 63.6 cc. These 85 Gm. of sugar, dissolved in 48 cc. of water, made 100 cc. of syrup, showing a contraction of 11.6 cc. in the process.

As other examples of contraction may be cited:
Sodium chloride, 30 Gm. in 100 cc. water contracts 3.11 per cent.
Potassium iodide, 85 Gm. in 100 cc. water contracts 2.49 per cent.
Potassium acetate 100 Gm. in 100 cc. water contracts 6.16 per cent.

It is interesting to note that ammonium chloride dissolves in water with little or no shrinkage in volume, while Lowry states that "caustic soda . . . actually appears to occupy a *negative* volume when dissolved in water."

A notable case of contraction as when alcohol and water are mixed in preparing diluted alcohol. This is sufficiently marked to be worthy of attention by the operator, as shown by an incident coming to the author's attention, in which a pharmacist, in preparing 40 gallons of diluted alcohol for a customer, mixed 20 gallons of alcohol and 20 gallons of water, bottled it without measuring, and was much grieved on receiving complaint from the customer that the quantity was several quarts short.

It is said that 50 volumes of ethyl alcohol and 50 volumes of water make 94.35 volumes of diluted alcohol while 50 volumes of methyl alcohol and 50 volumes of water make 98.5 volumes of fluid. Mendeljeff stated that alcohol and water exhibited the maximum contraction when 45.88 per cent alcohol was prepared and that this showed the formation of a compound consisting of one molecule of ethyl hydroxide. and three molecules of water.

Determination of Solubility.—Reference has been made in a preceding paragraph to the solubility of a solid in water and other solvents. This is done in several ways, the usual method being by weighing a certain quantity of the solid in a tared bottle, adding a certain quantity of water at a given temperature, usually 25° C., shaking until assured of a saturated solution, then carefully transferring the liquid to a quick-acting tared filter and then weighing the solid residue. In this way we learn the amount of the solid which has been dissolved, and the solubility of the solid can be easily estimated on the basis of the solubility of 1 Gm. of the solid; thus, if the experiment shows that 1 Gm. of salt dissolves in 3 Gm. of water, then the solubility is put down as one part in three of water. This method, however, is not exactly accurate, inasmuch as during filtration a certain amount of the solvent volatilizes, leaving a greater residue than that actually soluble. A more accurate way is to take a given quantity of the solution, evaporate same to dryness, and from this determine the solubility of the solid. In the latter case, however, the contraction of a solid in the solvent must be known, and this factor used in the determination of the solubility can be easily obtained by adding the substance to the liquid until no more is taken up. Thus if to 100 cc. of water at normal temperature a solid is added in 5-Gm. lots, the solubility of the salt can be estimated within 5 per cent, and to attain absolutely accurate results it is only necessary to repeat the experiment by dissolving in the water the amount of salt within 5 Gm. of supersaturation, and to add the rest of the salt in ½-Gm. lots until no more is taken up.

For very accurate determination of solubility recourse is had to the lysimeter of Dr. Rice, while a good method of determining the solubility of alkaloids by use of volumetric solutions has been suggested by Hatcher. Attention has been called to the fact that in order to avoid supersaturation in determining solubility the mixture of the solid and its solvent should be thoroughly agitated by means of a mechanical stirrer during the process of solution.

Sterilization of solutions will be discussed in Chapter LII.

Ampuls and ampul filling will likewise be discussed in Chapter LII.

Gaseous Solution.—While physically a solution of gas in a liquid differs but slightly from the solution of either a solid or a liquid, the mode of preparing a gaseous solution differs sufficiently from the solution of either a solid or a liquid to justify a special heading. In effecting the solution of a gas in water when the gas is freshly generated or supplied from a storage tank (in which form liquid carbon dioxide is used largely for charging soda fountains), it is first washed by passing through water and then conducting it through a tube reaching almost to the bottom of the container holding the liquid, and to insure solution it is best that the container be long and narrow. When the soluble gas is run into the liquid, it is noted at first that the large bubbles emerging from the end of the tube are absorbed before they reach the top of the liquid; as the solution becomes more and more saturated it is found that the bubbles are less dissolved, until finally it can be noted that the size of the bubbles on emerging from the top of the liquid is about the same as when emerging from the end of the tube. When this stage is reached, it is always advisable to remove the container with the liquid and shake vigorously, again pass gas through, and if it is found by this means that no more gas is being dissolved, the operation is complete.

A simple test of saturation of a liquid with a gas is by observing the behavior of the solution after agitation. Place the hand over the mouth of the container, and if, after each agitation and attempted removal of the hand from the mouth of the bottle, a suction is felt, it is a strong evidence that the solution is not saturated. If, on removing the hand, a pressure of the escaping gas is observed, it is a fair indication of complete saturation.

In some cases, before making a solution of the gas, it is essential that same be dried, that is, freed from water vapor, in which case, instead of running such gas through water, it is passed through concentrated sulfuric acid, calcium chloride, or other substance having great affinity for water, contained in appropriate flasks (Fig. 134). There are some gases (ammonia, for example) which cannot be dried with calcium chloride nor sulfuric acid, and in such cases the gas can be fairly well dried by passing it through a bottle containing absorbent cotton. An illustration showing apparatus used for gaseous solution is appended (Fig. 135).

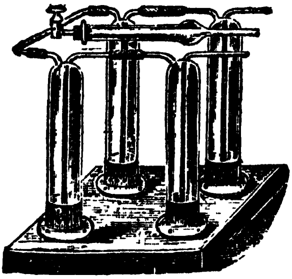


Fig. 134.—Apparatus for drying gases.

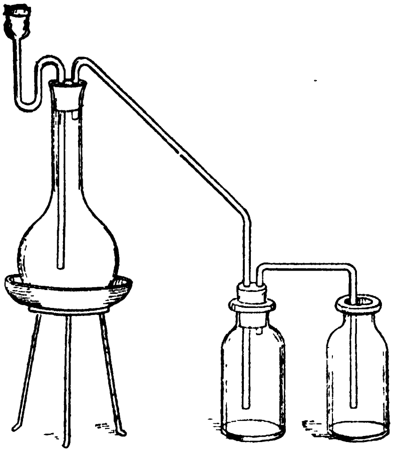


Fig. 135.—Gaseous solution.

LOTION

Lotion is derived from the Latin "lotio" (to wash), and means the removal of soluble impurities from insoluble substances by washing them with water or other appropriate liquid. Thus, in the last stage of purifying precipitated calcium carbonate, the precipitate contained on the filter is washed with water, while in making washed sulfur the sublimed sulfur is washed with a mixture of water and ammonia water. In other cases organic solvents, such as alcohol or ether, are used as wash liquids.

Apparatus used in lotion consists of funnel with a filter paper, or straining rack containing an appropriate strainer. (See Colation.) On this filter or strainer is thrown the substance mixed with the wash liquid, the latter, of course, passing through the strainer, the meshes of which hold back the insoluble matter. Upon the precipitate contained on the strainer, water or other wash liquid is poured until all of the soluble impurities have been removed, as can be ascertained by appropriate tests.

When only a small quantity of washing is required, the liquid is spurted upon the filter from a Spritz bottle, which consists of an ordinary pint chemical flask provided with a two-holed rubber stopper, through one hole of which passes a glass tube extending almost to the bottom of the flask, and above the cork bent at an acute angle and with the outside end drawn to a tapering point. Through the other hole is passed a shorter piece of glass tubing bent at an angle of 120–140 degrees. The water is removed from the Spritz bottle by blowing through the shorter piece of glass tube, when the increased pressure of air inside the flask will cause the liquid to pass through the longer glass tube, and emerge from the tapering end in a stream. If this stream be directed to the precipitate on the filter, the latter can be thoroughly and easily washed (Fig. 136).

Where large quantities of a liquid are needed for washing, it is a simple matter to devise a continuous process of washing, as shown in appended illustration (Fig. 137) in which it will be seen that a flask filled with water is inverted into the funnel containing the precipitate on the filter, upon which the liquid rushes until it reaches the mouth of the flask, when the flow ceases, owing to the inability of the air to pass into the flask. As the liquid of the funnel filters, its surface becomes lower than the mouth of the flask, thus permitting the entrance of air, causing a flow of the washed liquid from the flask until its mouth is again closed by the liquid in the funnel, and this continues until the flask is emptied, and that without danger of the liquid running over the edge of the funnel. Such simple apparatus is of great value in continuous filtration, in which case it is a simple matter to filter gallons of a liquid through a half-gallon funnel.

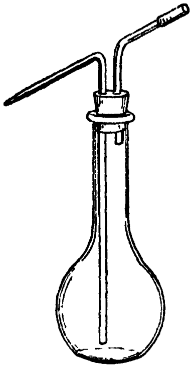


Fig. 136.—Spritz bottle.

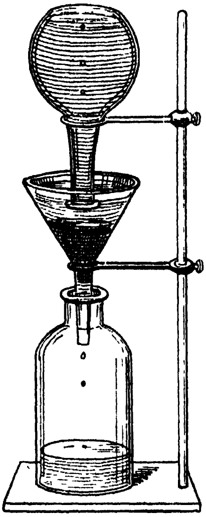


Fig. 137.—Continuous washing.

DECANTATION

In some cases it is more convenient to wash a precipitate by placing it in an appropriate glass vessel, such as a beaker or a flask, mixing thoroughly with a wash liquid, and allowing it to stand until the precipitate has completely subsided, and then removing the liquid by decantation; that is, by gently lifting the container and gradually tilting it until the major part of the liquid has been removed from the precipitate. It is manifestly impossible by this means to thoroughly remove all the liquid, as no matter how carefully decantation is continued, certain portions of the precipitate will be disturbed and flow out with the decanted liquid which, therefore, should be passed through a filter to collect the escaping precipitate. Repeated decantation, however, will enable us to remove most of the soluble matter from the precipitate. Thus, a precipitate contains 100 Gm. of soluble impurities: by treating with 1000 cc. water, the 100 Gm. of soluble matter will dissolve. By decanting this, it is possible to remove 900 cc. of the liquid without seriously disturbing the precipitate, and in 900 cc. 90 Gm. of soluble impurities will be contained. To the remaining liquid and the precipitate another 1000 cc. water is added, the product thoroughly mixed, and the precipitate allowed to settle. When 900 cc. of this second liquid are removed, it means that of the 10 Gm. of soluble substance remaining, 9 Gm. will have been removed, leaving with the precipitate but 1 Gm. of the original 100. The operation repeated, the 900 cc. of the decanted liquid will remove 0.9 of the remaining gram of the soluble impurity, and thus, after three such washings, but one one-thousandth of the original impurity remains.

Ordinarily, however, such thorough washing by decantation is not carried on, as it means the use of too much water.

Apparatus for decantation is the container mentioned above, consisting either of a pint flask or a beaker, provided with a pour-out or lip.

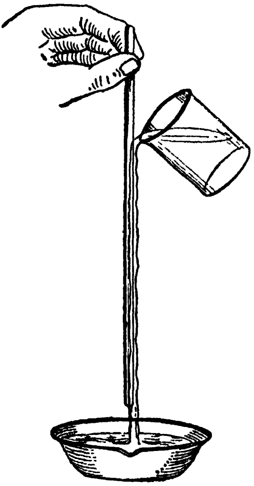


Fig. 138.—Decantation from beaker.

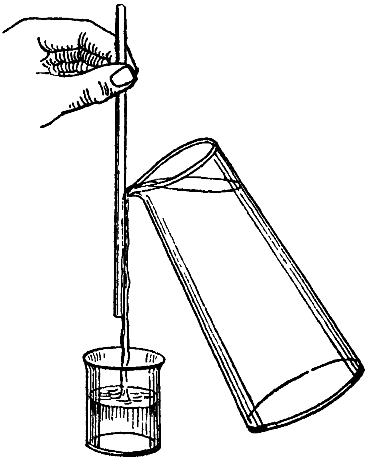


Fig. 139.—Decantation from precipitating jar.

To facilitate the removal of the decanted liquid, a glass guiding rod is used, such as was described on p. 108. The method of application is best shown by appended illustrations (Figs. 138 and 139). To avoid the possibility of any of the liquid being drawn over to the outside of the beaker by the capillarity of the glass, the edge of the beaker should be smeared with traces of some fat. The guiding rod is of great value in quantitative analysis, in which case every particle of the precipitate must be finally removed from the beaker and weighed. This is accomplished by slipping a small piece of rubber tubing over the end of the guiding rod and rubbing the sides of the beaker with same. Such rubber-tipped guiding rod is technically called a "policeman."

Where large quantities of liquid are to be decanted, recourse is had to the **syphon,** which consists of a bent tube, one arm of which is longer than the other. The shorter arm is placed in the liquid to be removed, and at the other end of the tube suction is applied (Fig. 140).

We take a syphon, immerse the short arm in water, and suck at the orifice of the longer arm. This has the effect of producing a partial vacuum in the tube—a pressure of air therein much less than the pressure of the atmosphere exerted upon the surface of the liquid in which the short arm is plunged. The result is that the superior pressure of the atmosphere forces the water into the syphon through the short arm, around the bend, into the long arm—this result, of course, being simultaneous with the suction applied at the end of the long arm. Entering the long arm, the liquid is subjected to the earth's gravitating force and falls downward. As each drop emerges from the syphon, were nothing to take the place occupied by that drop, a partial vacuum in the syphon tube would occur. Equilibrium—an exact balance between two parts of a machine or system—is the rule of nature, hence difference in pressure in the long and short arms of the syphon is not permitted, and the instant a partial vacuum is produced in the long arm, the water in the short arm and in the vessel into which the syphon dips, impelled by an atmospheric pressure, passes over to occupy the void.

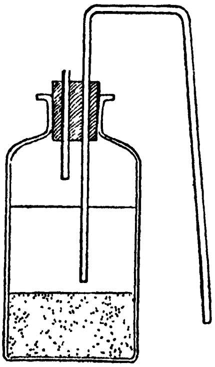


Fig. 140.—Syphoning.

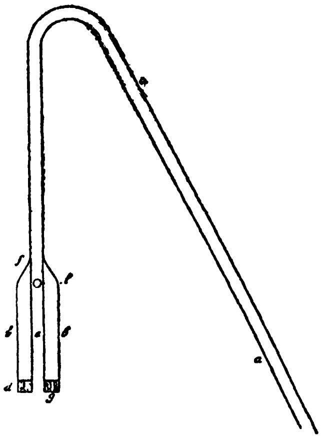


Fig. 141.—Automatic syphon

Just as rapidly as water emerges from the long arm, even so rapidly does water pass over from the short arm to take its place, and this condition continues so long as the short arm dips in water and the level of this water is higher than the level of the water that issues from the long arm.

Bon has devised an automatic syphon (Fig. 141). When the syphon is immersed, the fluid enters tube *a* much more rapidly than it does through *g*, *b* and *l*. The fluid entering tube *a* rapidly rises past *b*, places the air in *b* under pressure, forcing out the liquid above it, thus starting the syphon. A commercial form of this syphon is sold under the name of *Stransiphon*. Other special types of syphons have been devised with safety traps to obviate the danger of sucking corrosive liquids into the mouth.

COLATION

Colation is the technical name for the simple process of straining, by which term is meant the removal of coarse particles from a liquid by passing through a fabric the meshes of which are comparatively coarse. Thus, the domestic utensil, the colander, is useful in colation. In the same way a sieve can be used for the purpose of straining a liquid, but ordinarily the fabric through which the substance is passed is of some form of cloth. Among the various cloths used for straining are felt, flannel, muslin and cheesecloth.

Felt strainers are usually of conic form and yield a liquid as clear as if filtered. Equally useful is a strainer made of flannel (Fig. 142), and these are generally sewed together in the same conic form as the felt strainer, while the muslin and cheesecloth strainers are simply pieces of these fabrics fastened to a frame (Fig. 143). The latter consists of four pieces of wood, joined and studded with projecting nails, on which can be fastened the straining cloth. The latter should fit tightly to the frame without edges projecting, as in the latter case each filament of the cloth acts as a syphon and part of the liquid runs over the sides of the strainer to the container in a way that scarcely betokens pharmaceutic elegance.

In many cases of straining the operation has been aided by what has been termed "forcible straining," which means removing the straining cloth from the frame, gathering between the hands by a twisting movement the strainer and the residue thereon, and then expressing (p. 179). Straining is an imperfect operation, inasmuch as the strained liquid is rarely as clear as the careful pharmacist desires to dispense; hence, in most pharmaceutic operations filtration is preferable.

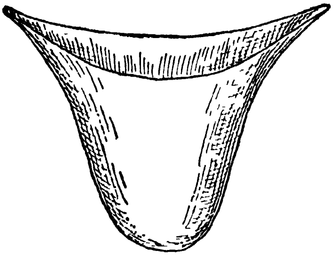


Fig. 142.—Leg-of-mutton strainer.

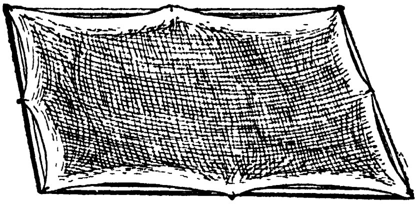


Fig. 143.—Strainer on frame.

FILTRATION

Filtration is a nearly perfect variety of straining; in both processes the operation of clearing the liquid being purely mechanical. As an illustration bringing this forcibly to mind, let us imagine we have a ditch of dirty water in which are pieces of wood (large and small), waste paper, and suspended mud. The ditch narrows to an underground drain, and, in order that the drain does not become clogged up, a grating is placed at its entrance. This grating is perhaps only six or seven iron bars, but as the water passes by them, some of the wood and paper, not able to pass through the spaces, remains on the grating. Suppose we take that water which has passed through the grating into the drain-pipe and examine it. It will be found as dirty as before, save that the larger chips and the masses of paper are removed. It contains bits of straw, slivers of wood, and fragments of paper pulp that were small enough to pass through the grating. This unsightly mixture we pour on a strainer of cheesecloth. The meshes in this are much smaller, of course, than the spaces in the grating, and the liquid emerges from the strainer much clearer, the strainer having kept back straw, wood-fiber, and paper pulp, along with considerable of the muddy sediment. However, it is still far from clear; the suspended mud in very finely divided form having passed through the meshes of the cheesecloth, which were not quite small enough to retain the minute particles. So we take the cloudy liquid and pass it through filtering paper, the meshes (the pores) of which are so small as hardly to be seen with the naked eye. This process usually completes the work of removing the undissolved particles, the liquid emerging from the filter perfectly clear.

Let it here be said that modern sanitary engineering has shown that filtration of water through long layers of sand removes not only visible dirt, but can, if properly carried out, remove bacteria that cause disease. Notable among such efforts are the water systems of a number of our American cities.

The substance which removes the impurities is called the filtering medium, and the clear liquid, the *filtrate*.

Apparatus used in filtration consist of the bottle or other container into which the filtrate drops and the container holding the filtering medium. The latter in small operations consists usually of a funnel, while in large processes of filtration it consists of earthenware crocks, or tanks of iron, wood, or masonry. The latter being beyond the province of this work, reference will be had solely to *funnels*.

Funnels consist of conic vessels of glass, porcelain, or metal, although the latter should be carefully avoided in delicate pharmaceutic operations. To secure the best success from a funnel, it is necessary that the cone shall be at an equilateral triangle, as otherwise folded filter paper will not accurately fit it. Of the many varieties of funnels suggested for pharmacists' use, reference can be had here merely to a few types. It has been the writer's experience that just as good results are obtained by using a plain glass funnel (Fig. 144) as can be secured with more elaborate varieties, the main point in successful filtration being the correct folding of the filter paper. A very popular form of funnel is the one with the ribbed interior, to permit the passing down of the filtered liquid (Fig. 145). This, however, can be accomplished just as well by the plaits of a carefully folded filter.

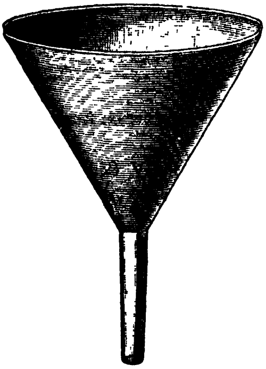


Fig. 144.—Plain funnel

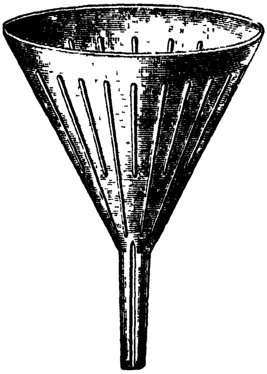


Fig. 145.—Ribbed funnel

The same funnel is provided with a groove on the under side of the neck of the funnel to permit the exit of air from the bottle into which the liquid is filtered. It is better pharmacy, however, not to place the funnel directly in the neck of the receiving bottle, but to support it on a ring of the retort stand (Fig. 146).

If circumstances are such that the funnel must be placed in the neck of the bottle, some provision for access of air must be made, and this is done by interposing between the neck of the funnel and that of the receiving bottle a piece of cord; otherwise the air within the bottle becomes compressed as the liquid passes into the bottle until either the liquid ceases to filter through or the air, in forcing its way out, pushes with it a certain quantity of the filtered liquid to the outside of the receiving flasks, producing an untidy operation.

This is particularly the case if the neck of the funnel is either too large or too short. It should enter completely the neck of the bottle and pass within the wider portion of same.

The **filtering medium** may consist of paper, cotton, cellulose pulp, felt, asbestos, woven metal, sand, earth, coke, sawdust, cork, carbon, silica, porcelain or porous stone, the first two being generally used in retail pharmacy.

Paper filters consist of sheets of unsized paper, which, when properly folded, form a conic bag on which the liquid to be filtered is poured. In commerce we find two varieties of such filter paper, one being gray and the other white. The latter is more expensive than the gray, but is preferable for pharmaceutical use.

The filter paper can be folded in two ways (usually termed *plain* and *plaited filters*), and each has its peculiar use, plain filters being indicated when the precipitate is desired, and plaited filters when the filtrate is sought for.

In making a plain filter, the paper is folded but twice, in each case the sheet being divided exactly in half. The result is a perfect cone, with one thickness of paper on one side and three thicknesses on the other, which naturally produces unequal filtration. In order to equalize, we frequently use two such plain filters, so alternating that both sides will be four layers of the filter paper. At its best a plain filter does not remove the liquid with rapidity because the paper lies flat against the surface of the funnel, and the only place through which the filtrate can readily pass is at the point which lies exposed at the neck of the funnel. Therefore, for rapid filtration, a plaited filter is best.

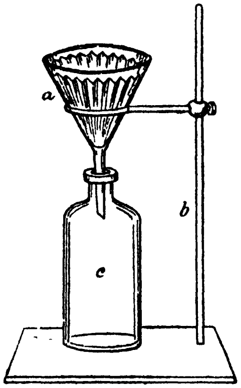


Fig. 146.—Correct filtration: *a*, funnel; *b*, filtering stand; *c*, receiving bottle.

In the plaited filter the paper is so folded as to make a cone of equal thicknesses on all sides, and is also provided with canals through which the filtrate can run. The plaiting of a filter is a matter of considerable skill, and there is but one correct way to fold a successful filter. To understand thoroughly the method it is necessary to accompany the explanation by illustrations (Fig. 147). The circular piece is folded exactly in the center (*a*). This semicircle is again folded in its center (*b*). The semicircle is then opened and half of the semicircle is folded upon the central crease (*c*). This gives one fourth of the circle divided into eighths, and these eighths are now folded into sixteenths (*d*) each fold being against the upper surface of the filter paper.

Attention is then paid to the other fourth of the circle, it being folded exactly as was the first fourth, and as a result it being folded into sixteenths as shown in (*e*). These sixteenths are then divided into thirty-seconds by folding each back on itself, and when finished the unopened filter should present the appearance of (*f*), that is, a series of perfectly symmetric plaits, only two of which will rest against the edge of the funnel, and these can be removed by folding into sixty-fourths, as (*g*). The observance of the following details will contribute to attaining the ideal in filtration:

First, the folds of the filter should not be permitted to extend to the point of the filter, but in plaiting the filter the crease should be made from the point toward the edge, a finger being kept on the point to prevent the creasing of same. The necessity of sparing the point can be understood when it is appreciated that every crease in the piece of paper contributes to the weakening of same, and, therefore, the passing of sixteen creases across the central point forming the tip of the filter is apt to so weaken it that it will break as soon as the liquid is poured upon it, the greatest pressure of the liquid being exerted on the filter tip.

Second, the filter should be moistened before filtering. This opens the pores of the filter, rendering easier the passage of the liquid through the filter. It is needless to say that the filter should be moistened with the liquid which is the solvent for the drug intended to be filtered. Thus, to moisten with water a filter through which it is intended to pass essence of ginger would be doing much more harm than good. The moistening of such a filter should be done with alcohol.

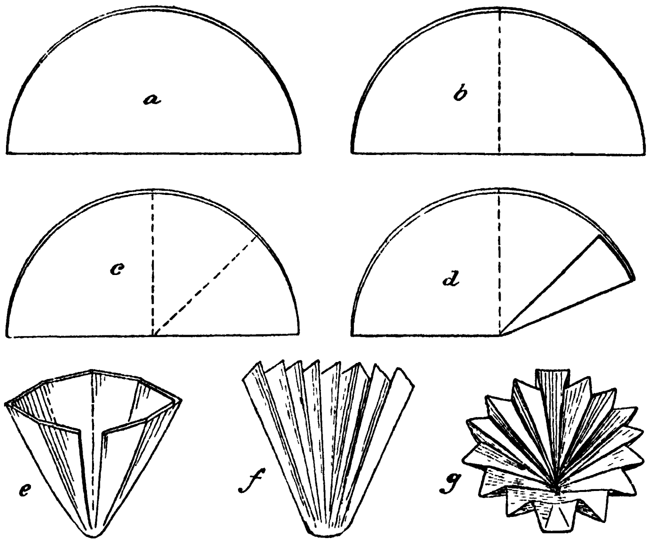


Fig. 147.—Folding plaited filter (see text)

Third, when the filter is moistened, it is advisable to push the tip of the filter fairly well down into the neck of the funnel. This serves to strengthen the filter tip.

Fourth, in pouring the liquid on the filter, avoid throwing it directly on the tip, but gradually pour it upon one side of the filter, as otherwise the force of the fall is apt to rupture the paper.

Fifth, the paper should not project above the funnel. It is a human failing to fill the filter as completely as possible, and in case the paper projects over the side of the funnel, the actual level of the liquid may be above the top of the funnel, and a rupture of the paper brings disastrous results. The chief reason, however, for this rule is that the projecting paper affords considerable surface exposed to the air, thereby producing spontaneous evaporation, with accompanying loss of the liquid. This is particularly the case when the liquid to be filtered is volatile.

Cotton Filter.—In many cases of simple filtration all that is necessary to remove the insoluble matter is the passing of the liquid through a pledget of cotton placed in the neck of the funnel. This method of filtration is one which should be practiced more frequently behind the prescription counter than is usually the case. Every prescription calling for a solution should be dispensed absolutely clear, and to insure this the finished solution should be filtered through cotton before dispensing. If three or four funnels of various sizes be kept within reach and a package of absorbent cotton be kept in the drawer of a prescription case, such filtration is simple, the custom of the writer being to filter directly into the bottle in which the prescription is dispensed.

Asbestos Filter.—Instead of a plug of cotton, a similar plug of purified woolly asbestos inserted in the neck of the funnel affords an admirable method for the filtering of strong acid or alkaline liquids, which would destroy filter paper or cotton. Such asbestos wool can now be easily obtained at moderate cost, and should share a place in the drawer in which the absorbent cotton is kept. By means of the asbestos it is a very simple matter to filter a solution of sodium or potassium hydroxide.

Sand and **stone filters** are used in large operations only, such as filtering drinking water. The sand filter usually consists of a vat in which are placed alternate layers of sand, charcoal, and gravel, to a depth of 3 feet. Upon this the water is thrown and percolates through to the bottom, and is drawn off by means of a faucet. In the filtration of city water supply 20-foot filter beds are not infrequent.

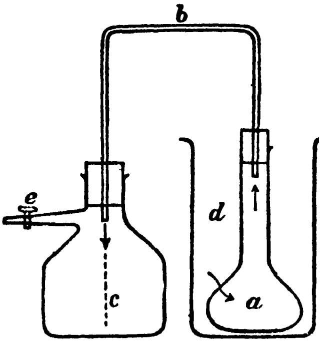


Fig. 148.—Porous flask filter.

Many patent varieties of stone filters are in the market. They consist of porous stones cut into shapes suitable for the container, and through which the liquid passes. A very convenient and small modification of the stone filter is the porous flask (Fig. 148), which is attached to a syphon and placed in a vessel containing the liquid desired to be filtered. The play of the syphon once established, the liquid passes from the original container through the porous flask, and emerges from the syphon completely filtered. In some modern filter presses, disks of porous material are employed. Small disks or cones of such material (*alundum*, for example) are used in filtration operations in the chemical laboratory.

Filtration through Absorbent Powder.—This is a modification of filtration where the separation of the insoluble matter is facilitated by the use of some powder that has the property of adsorbing such material. On a small scale the powders employed are magnesium carbonate, talc, infusorial earth, silica gel, etc., these being used to aid filtration through paper. In this way some of the official aromatic waters are prepared (p. 196).

Filtration through Porcelain.—In making bacteriological products such as serums and vaccines and in sterilizing certain types of solutions which would be adversely affected by heat or chemicals, filtration through porcelain has been found effective. The type of filter in common use is known as the Berkefeld filter.

Adsorption is now recognized as an important phenomenon in physical chemistry; the holding back of the matter by absorbent substance being akin to atomic attraction (p. 384). Recent experiments show that in filtration through paper, adsorption of the solute by the paper frequently assumes considerable proportions. In filtration through charcoal or kaolin adsorption is a common phenomenon and must be carefully guarded against. (See also p. 162).

Volatile Filtration.—In case the liquid to be filtered is volatile, precautions must be taken to prevent undue evaporation. This is usually accomplished by placing the filter paper in a funnel considerably larger than itself, covering the funnel with a sheet of rubber or plate of glass, while the neck of the funnel fits into a cork stopping the neck of the receiving bottle. In order to permit exit of air from the receiving bottle and ingress of air into the top of the funnel, these two may be connected with a rubber or glass tube in the same way as explained under Volatile Percolation (p. 191).

Hot Filtration.—Some liquids can be filtered only when quite hot, and with certain easily fusible solids the best method of purification is by filtering them while in the molten state; such, for example, is the case with wax. In all such cases the funnel containing the filtering liquid must be kept warm, and for such purposes various forms of hot filtration apparatus have been devised (Fig. 149). These usually consist of water baths with the conic holes in which the funnel will fit. A cheap and practical form of such hot filtration apparatus, devised by Hatcher, consists of a tinned iron funnel with its neck closed by a perforated cork, through which passes the neck of a glass funnel. In the space between the inner wall of the metallic funnel and the outer wall of the glass funnel water is placed and kept warm by means of a Bunsen burner (Fig. 150).

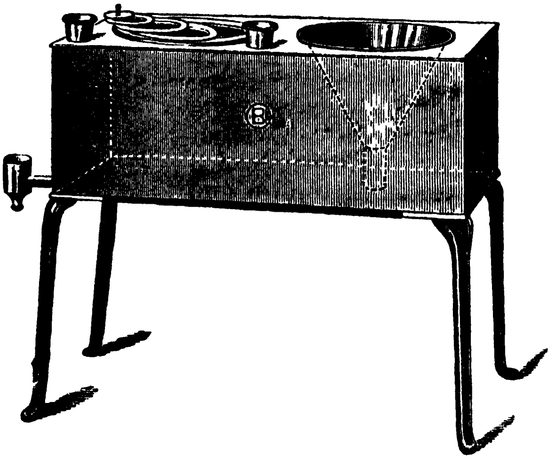


Fig 149 —Hot filtration bath

Rapid Filtration.—In many cases of ordinary processes of filtration the liquid filters through so slowly that some means to increase the flow is necessary. This is usually accomplished by fitting the receiving bottle with a two-holed rubber stopper, through one perforation of which the neck of the funnel passes, while the other is fitted with a bent glass tube connected with an apparatus which will rarefy the air within the receiving bottle. A special form of receiving bottle is obtainable in which the air is drawn off by a tube connected from the side of the bottle (Figs. 151

and 152). In such cases the pressure of the atmosphere acting on the surface of the liquid in the filter is greater than the pressure within the receiving bottle, and hence forces the liquid through the pores of the filter into the receiving bottle, and that frequently with such great force as to rupture the filter paper unless some means is taken for its protection. This is usually accomplished in filtering liquids in quantitative chemistry by fortifying the tip of the filter paper with a cone of perforated platinum. Such quantitative precipitates, however, can best be separated from the liquids in rapid filtration by use of the Gooch crucible filter (Fig. 153), which consists of a porcelain crucible provided with a perforated

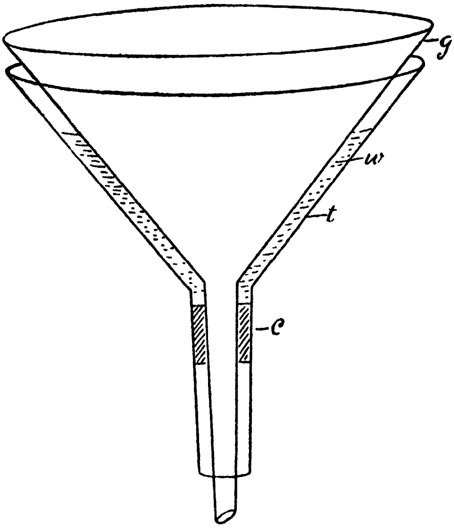


Fig 150.—Funnel for hot filtration: *g*, glass funnel; *t*, tin funnel; *w*, water; *c*, cork (Hatcher and Sollmann).

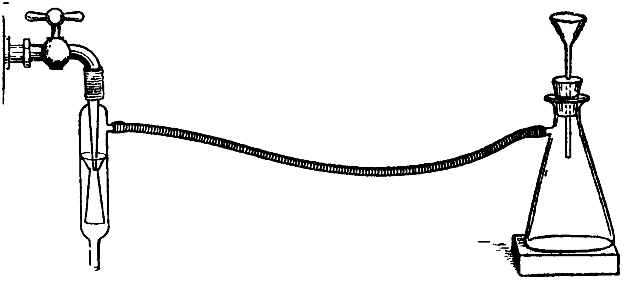


Fig 151.—Rapid filtration

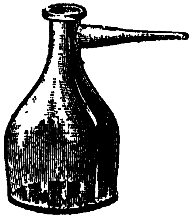


Fig. 152.—Filtering flask.

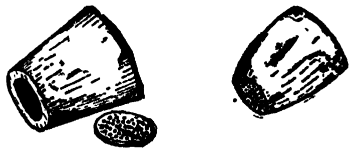


Fig. 153.—Gooch crucibles.

bottom in which is inserted a mat of asbestos wool and this, by means of the large rubber tubing, fitted to the smaller funnel connected with filtering flask (Fig. 154).

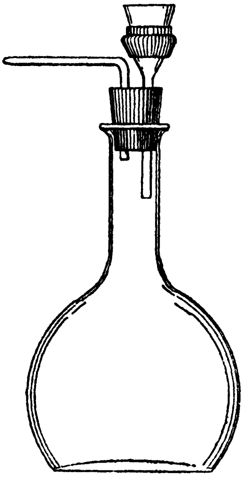


Fig. 154.—Gooch crucible in filtering flask.

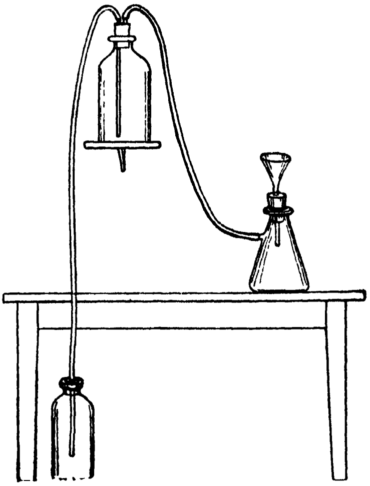


Fig. 155.—Syphon filtration

Gooch crucibles are now available with a filtering disc made of porous glass. It is now possible to make uniform glass filters with a mean pore diameter of 1.5 microns.

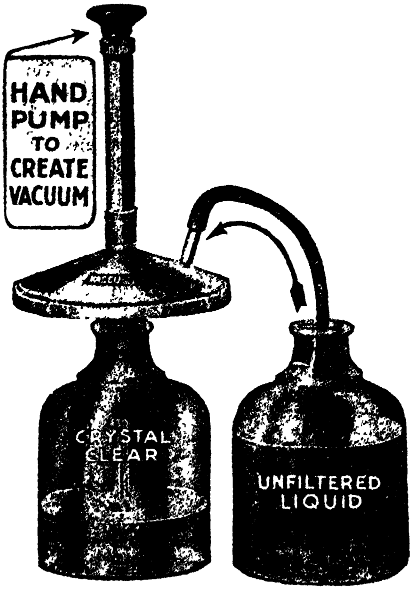


Fig. 156.—Bryden vaccu-filter.

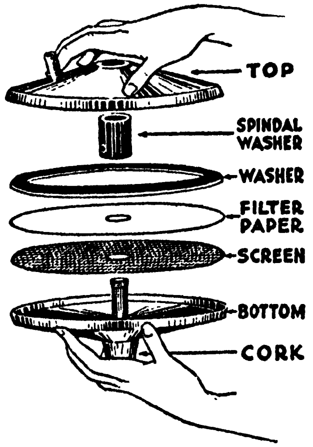


Fig. 157.—Bryden vaccu-filter (dissected).

The rarefaction of the air within the flask can be accomplished with the water pump pictured on p. 110, or, in its absence, sufficient air can be removed by the simple expedient of syphon suction.

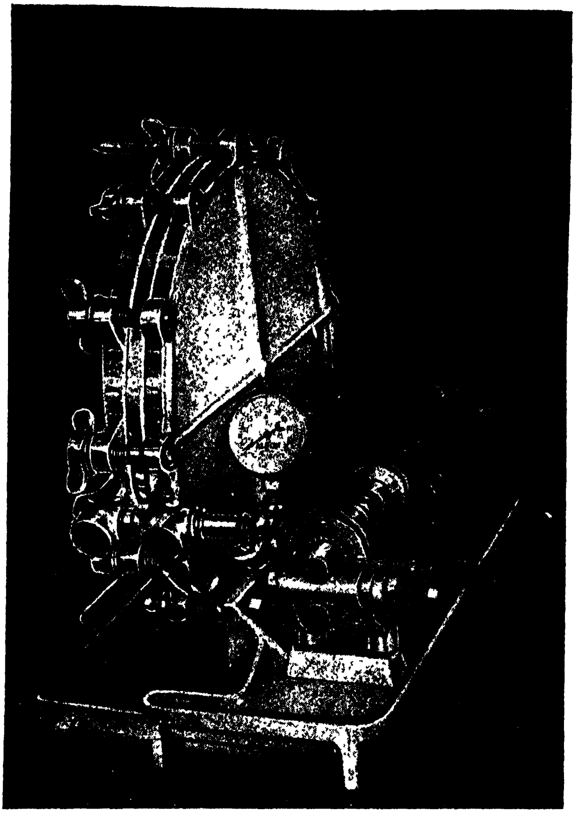


Fig 158.—Alsop "Hy-speed", asbestos disc filter. Bench type. (Courtesy of Alsop Engineering Corp)

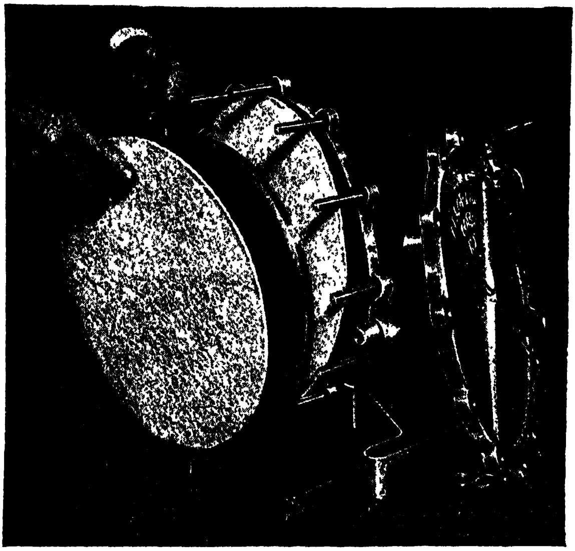


Fig. 159.—Showing method of placing asbestos discs in Alsop "Hy-speed" asbestos disc filter. (Courtesy of Alsop Engineering Corp.)

The apparatus consists of two 1-gallon jugs, each fitted with two-holed cork stoppers. Through the orifices of each stopper pass bent glass tubing, one extending to the bottom of the jug, the other only a few inches below the under side of the stopper. In the operation one jug is filled with water, placed on a table, and connected with the other jug placed on the floor by rubber tubing attached to the long glass tube of each jug. The small glass tube of the upper jug is fitted by thick rubber tubing to the end of the aspirator, and the water in the jug is made to syphon over into the lower jug, thus producing suction within the upper jug and the filtering bottle. When all water has run into the lower jug, the position of vessels is reversed and the operation continued (Fig. 155). A convenient form of vacuum filter is illustrated in Figs. 156 and 157.

For the filtration of large quantities of liquids in manufacturing processes a number of types of power apparatus have been devised. The most important of these are plate filter presses provided either with canvas filter cloths or with special filtering discs made of porous mineral materials (Figs. 158 and 159). Chemical engineers have been able to reduce the operation of these filters to the terms of mathematical formulas. An interesting type of a vacuum filter is the Louisville machine. A third type especially designed for viscid liquids is built on the principle of centrifugal cream separators (Fig. 160).

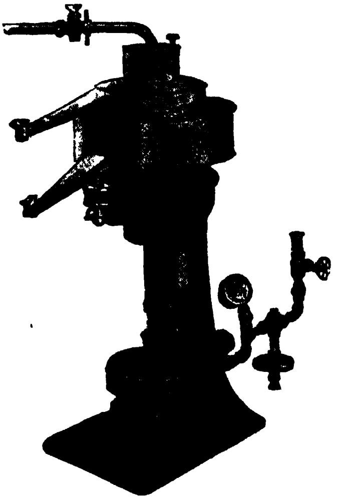


Fig. 160.—The De Laval clarifier and filter.

BIBLIOGRAPHY

Solution.—Linebarger, Science, 20, 1892, 352; Trevor, Am. Ch. Jl., 15, 1893, 137, 290; Reychler, Jl. Ch. Soc., 64, 1893, 315; Arrhenius, B., 27, 1894, 6, 407; Eccles, A.Ph.A., 46, 1898, 468; Jones, Jl. Frank. Inst., 175, 1912, 217; *ibid.*, 176, 1913, 677; Brockman, Jl. Soc. Ch. Ind., 44, 1925, 501; Flint, Jl. Wash. Acad. Sci., 22, 1932, 97.

Solvents.—Lloyd, Ostwald and Haller, Jl. A.Ph.A., 19, 1930, 1076; Gross and Saylor, Jl. Am. Chem. Soc., 53, 1931, 1744.

Solubilities.—(General) Lloyd, Jl. A.Ph.A., 6, 1917, 940; Flottmann, Zt. analyt. Ch., 73, 1928, 1; Schnellbach and Rosin, Jl. A.Ph.A., 18, 1929, 762 and 1230; *ibid.*, 20, 1931, 227. (Glycerin solubilities) Ossenkowski, A.Ph.A., 55, 1907. 902 and 56, 1908, 353; Hollemann, Zt. phys. Ch., 12, 1893, 133; Holm, Pharm. Weekbl. through C.A., 15, 1921, 2962 and 3181; Bancroft, Jl. Frank. Inst., 185, 1918, 226; Birza, Ph. Weekbl., 67, 1930, 729.

Volume Changes on Solution.—Mendelejeff, B., 41, 1908, 4790; Anon., Merck's Rep., 19, 1910, 172; Candidus, A.Ph.A., 27, 1879, 709; Bolenbaugh, Jl. A.Ph.A., 5, 1916, 38; Lowry, Jl. Soc. Ch. Ind., 47, 1928, 1260.

Solubility Estimations.—Rice, Jl. Am. Ch. Soc., 16, 1894, 715; Hatcher, A.J.P., 74, 1902, 136; Paul, Arch. d. Pharm., 239, 1901, 48.

Percentage Solutions.—Bradley, Jl. A.Ph.A., 6, 1917, 955; Am. Dr. 94, July, 1936, 56; Burt, Jl. A.Ph.A., 16, 1927, 1198.

Syphons.—Goedecker, Ch. Zt., 36, 1912, 422; Pelle, Ch. Weekbl., through C.A., 15, 1921, 1642; Fuchs, Chem. Fabrik, 3, 1930, 173.

Filtration.—(History) Bolton, Merck's Rep., 11, 1902, 463. (Funnels) Lyons, Am. Dr., 53, 1908, 345. (Upward filtration) Symes, Ph. Jl. [3], 13, 1883, 937. (Rapid filtration) Gooch, Ch. News, 68, 1893, 8; Anon., Ch. Zt., 34, 1910, 660; Blackman, Ch. News, 104, 1911, 30; Prausnitz, Ch. Zt., 53, 1929, 935 and 955; Schugt, Apoth. Zt., 45, 1930, 393. (Automatic filter) Austin, Dr. Circ., 64, 1920, 245. (Adsorption) Lloyd, Jl. A.Ph.A., 5, 1916, 1053; Scoville, Jl. A.Ph.A., 5, 1916, 506; Gordon, J. Phys. Ch. through C.A., 8, 1914, 2833; Krantz, Jl. A.Ph.A., 45, 1923, 864 and *ibid.*, 20, 1931, 784; Kolthoff, Zt. analyt. Ch., 76, 1929, 360.

Filter Paper.—(Manufacture) Fornstedt, Paper, 10, 1913, 17. (Quality) Greenish, Yearbook Pharm., 1876, 598; Keenan, Am. Dr., 41, 1913, 7. (Texture), Scoville, Dr. Circ., 51, 1907, 458. (Folding) Hehner and Richmond, Analyst, 13, 1888, 2.

Suction Pump.—(History), Anon., Sci. Amer., through Am. Dr., 16, 1887, 121.
Commercial Filtration.—(Mathematics of) Sperry, Met. Ch. Eng., 17, 1917, 161; Hinchley and co-workers, Jl. Soc. Ch. Ind., 45, 1926, 1T; Van Gilse and co-workers, *ibid.*, 49, 1930, 444; Ruth and co-workers, Jl. Ind. Eng. Ch., 23, 1931, 850. (Operation) Faber, Jl. Soc. Ch. Ind., 39, 1920, 21T; Alliott, *ibid.*, 39, 1920, 261T; C.C.D., Ph. Jl., 110, 1923, 588; Ure, J. Soc. Ch. Ind., 43, 1924, 136, 678 and 975; Runyon, Jl. Ind. Eng. Ch., 19, 1927, 687; Clark, *ibid.*, 19, 1927, 688.

CHAPTER VIII

CLARIFICATION, DECOLORIZATION, AND SEPARATION OF IMMISCIBLE LIQUIDS

CLARIFICATION

CLARIFICATION is the process of clearing a liquid without the aid of filtration. As filtration is a simple and thorough operation, clarification is substituted for it only in cases where filtration is difficult, if not impossible, as in the case of mucilaginous and other viscid liquids which will not pass through the pores of a filter or where the quantity of fluid is too great for ordinary filtration. The clarification of liquids, whenever possible, is accomplished by means which are purely mechanical; clarification by means of chemicals not being recommended because of danger of alteration of the liquid during the process. The apparatus for clarification is usually of the simplest character, consisting generally of a vat, kettle or dish, and some form of strainer through which the liquids are passed to remove it from the solids. Clarification is accomplished in the following ways:

1. *Heating.*—In many cases the liquid to be clarified is turbid by reason of suspended or partially dissolved albumin or wax. In such cases heating usually accomplishes clarification by coagulating the albumin or by causing the waxy substance to liquefy and rise to the surface. After such cases of clarification the cooled liquid is either strained, or the separated solids float on the surface (scum) and are removed by skimming. An illustration of this kind of clarification is the process of clarifying honey, as given in the Pharmacopœia of 1880.

2. *Increasing Fluidity.*—In some cases suspended particles of dirt, grit, and straw make turbid a liquid which is so viscid that these particles can neither rise to the surface of the liquid if lighter than same, nor sink to the bottom if heavier. This can be remedied by diluting the liquid with water until sufficiently limpid to permit separation of the solid matter and then evaporating the excess of water.

3. *By Use of Albumin.*—The method given above is not always satisfactory, as frequently it is inconvenient to evaporate the exeess of water, and, moreover, it is often the case that the particles do not separate of their own volition. The separation of these particles can be facilitated by thoroughly mixing white of egg with the liquid and then heating the mixture, when the albumin coagulates and rises to the surface of the liquid, carrying with it the mechanical impurities, which are skimmed off along with the solidified albumin. By this process boiled coffee may be rendered clear.

4. *By Use of Milk.*—In the above operation milk is sometimes substituted for albumin, this acting the same way by reason of the coagulation of the casein it contains.

5. *Paper Pulp.*—A similar mechanical separation of the particles can by accomplished by tearing filter paper into shreds, mixing it thoroughly with the liquid, and heating. When the paper rises to the surface it carries with it the suspended particles, which are removed by skimming. The method of clarifying honey that was formerly official combined the use of paper pulp with increasing the fluidity of the liquid.

6. *By Sedimentation.*—If the particles rendering the liquid turbid are sufficiently heavy, they will settle to the bottom of the containing vessel, even though the liquid is quite viscid, if sufficient time is given to accomplish the separation. This slow method of separation is called *sedimentation,* and the insoluble matter finally settling at the bottom of the vessel is called the *sediment.* The term *precipitate,* frequently applied to the sediment, is incorrect, as by precipitate we mean insoluble matter which has been in solution, whereas the particles composing sediment have never been dissolved.

7. *By Use of Gelatin.*—Gelatin is employed for clarifying liquids containing tannin, the action in this case being chemical, and not mechanical. Gelatin forms with tannin an insoluble combination, similar to leather. (See page 951.)

8. *By Fermentation.*—This is a method of clarification, the application of which is limited to the preparation of fruit juices used at soda fountains. The preparation of these is a simple matter. Fruit is crushed either by pounding in a tub or by means of a fruit crusher or grater, and the pulp allowed to stand in a comparatively warm place for twenty-four hours. Partial fermentation is begun, and the slight change in the chemical character effects a separation of the clear juice from the pulp and albuminous matter, permitting the easy separation of the juice from the insoluble matter by straining, and the strained juice is then placed in bottles, corked, and sterilized by submitting to the action of boiling water for half an hour or more. If preferred, the sterilization can be omitted and the fruit juice preserved by the addition of alcohol. Some of the commercial juices are preserved by the addition of certain antiseptics, but in most States the addition of these preserving agents is prohibited by legislative action.

DECOLORIZATION

Decolorization is the process of removing color from a substance, and is usually accomplished by macerating the solution with animal charcoal for several days and then filtering. Charcoal, either animal or vegetable, is the only convenient substance possessing this decolorizing property, due to the powers of adsorption it possesses. This adsorbing ability applies not only to coloring matter, but also to glucosides, alkaloids, and bitter principles, hence in decolorizing decoctions of the drugs containing the latter substances by use of animal charcoal they suffer some loss in active principles. (See p. 435.) Activated charcoal (see page 434) has officially replaced wood and animal charcoal formerly both official.

Absorption and *adsorption* are words used to designate the taking up of liquids or gases by solids. In adsorption it is supposed that the substance taken up adheres to the surface and does not penetrate the adsorbent. The adsorption is due to cohesion, to surface tension changes and largely to chemical forces.

SEPARATION OF IMMISCIBLE LIQUIDS

By immiscible liquids we mean two liquids which do not dissolve in each other, for example, water and oil, and in cases where these two are brought together, it is very frequently useful to have a means of separating them readily. In some cases immiscibility is intentional. For example, in alkaloidal assays, we pour into an alkaline aqueous solution some "immiscible" solvent such as ether or chloroform in order that the alkaloid can be taken out of the aqueous layer by the added solvent. (See Part V.) Immiscible liquids are separated by several methods. In case the amount of one of the liquids is very small, it can be separated from the other by means of a *pipette*, one end being placed in the liquid, which is drawn into the pipette by means of suction (Fig. 161).

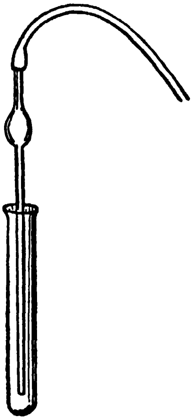


Fig. 161.—Separation of immiscible liquids with pipette.

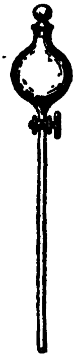


Fig. 162.—Separatory funnel.

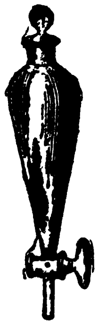


Fig. 163.—Squibb's separatory funnel.

A similar form of crude separation can be accomplished more thoroughly by a cheap glass *syringe*, the suction in this case being accomplished by moving the piston. Both these means of separation, however, are very primitive, and should be used only in emergencies. Thorough separation can be accomplished by the inexpensive *separatory funnel* (Figs. 162 and 163), which consists of a glass bulb provided with a glass stopper and terminating in a tapering tube to which is fitted a glass stopcock. For those economically inclined, an ordinary glass funnel can be used

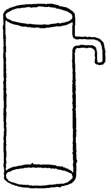


Fig. 164.—Florentine receiver for heavy liquids.

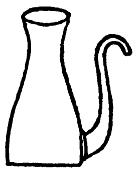


Fig. 165.—Florentine receiver for light liquids.

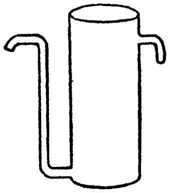


Fig. 166.—Florentine receiver combined.

as a separatory funnel by fitting in the neck of same a velvet cork stopper fitted with a glass rod, and allowing the liquid to run out from the funnel by raising the stopper and pressing it down when the last portion of the heavy liquid has been separated. Considering, however, the low price of a separatory funnel, the use of this crude apparatus is hardly justified.

One immiscible liquid can be crudely separated from another by means of a *syphon*, but to this method the same comments can be applied as to separating with a syringe.

By Florentine Receiver.—For the separation of a quantity of immiscible liquids too large for the separatory funnel, recourse is had to the Florentine receiver (Figs. 164, 165, and 166), this being used in the steam distillation of substances containing volatile oils to separate the volatile oil from the water which accompanies it in the distillation. As shown in illustrations, two forms of such receiver are used, accordingly as the oil is heavier or lighter than water, each apparatus being so arranged as to cause the flowing out of the water and retention of the oil in the receiver, while the third illustration shows a receiver adapted to either light or heavy oils.

A crude method of separating chloroform from large quantities of water, such as is sometimes required in the extraction of alkaloids from drug decoctions by shaking with chloroform, is by agitating the mixture in a 5-gallon demijohn or can, and suddenly inverting same into a quart or half-gallon wide-mouthed bottle, and when the chloroform has completely separated into the jar, the demijohn is removed and the chloroform separated from last small quantities of water by use of an ordinary separatory funnel.

BIBLIOGRAPHY

Clarification.—(General) Dieterich, Am. Dr., 19, 1888, 211. (Milk) Foulon, A.J.P., 65, 1893, 15. (Paper pulp) Foulon, Jl. de ph. et ch., 26, 1892, 207.

Adsorption.—Bancroft, Jl. Frank. Inst., 185, 1918, 199; Mathews, Physiol. Rev., through C.A., 16, 1922, 425.

Separation of Immiscible Liquids.—(General) Currier, A.Ph.A., 32, 1884, 39; Arny, Pharm. Era, 25, 1901, 700. (Florentine receivers) Gildemeister-Hoffmann-Kremers, 1900, 70. (Separatory funnels) Fritz, Ch. Zt., 38, 1914, 712; La Wall, Jl. A.Ph.A., 3, 1914, 498; Luther, Zt. angew. Ch., through C.A., 15, 1921, 1833.

CHAPTER IX

PRECIPITATION, CRYSTALLIZATION, GRANULATION, EXSICCATION, AND DIALYSIS

PRECIPITATION

PRECIPITATION is the process of separating a solid from its solution by the aid of physical or chemical action. The substance so separated is called a *precipitate;* the chemical producing this precipitate is called the *precipitant,* while the liquid remaining above the precipitated substance is termed the *supernatant liquid.*

As mentioned in the last chapter, a precipitate differs from a sediment in that a precipitate is separated out from its former state of solution, while a sediment has never been dissolved. In order to precipitate a substance it is necessary to first get it into solution. On the other hand, the precipitated substance is, in the nature of things, a substance insoluble in water, and must, therefore, be dissolved by special agents, the act of solution frequently bringing about a chemical change.

Precipitation may be due to chemical or physical causes. The most important phase of precipitation is that involving chemical action, wherein the two reacting substances are dissolved in separate portions of water, and on mixing these solutions an insoluble body will be formed and precipitated.

But we have precipitations that are due to purely physical causes. Thus from a hot supersaturated solution on cooling will be precipitated the excess of dissolved substance. Likewise, solution of such substances which are more soluble in cold water than in hot (like lime) will be precipitated when they are heated, such cases being examples of precipitation through change in temperature. We have learned that substances may be soluble in one liquid and insoluble in another; thus, gum arabic dissolves in water to form a colloidal solution but is insoluble in alcohol. If alcohol is added to a solution of acacia, it diffuses through the water and the acacia is precipitated, an example of precipitation through change in solvent.

Objects of Precipitation.—We precipitate substances chiefly to *purify* same. As will be noted later, the purification of chemicals which are soluble is easily effected by crystallization, and likewise, the purification of insoluble chemicals is generally accomplished by precipitation, and in both cases the act of purification is accomplished by first bringing the substance into solution. Therefore, in precipitation we dissolve a substance in some way, usually by changing the identity of the chemical. The solution thus obtained is rendered free from insoluble extraneous matter by filtration, and to the filtered liquid is added the appropriate precipitant, which converts the chemical into the insoluble form desired, leaving the soluble impurities in the supernatant liquid.

Another object of precipitation is to *obtain the substance in fine powder*, the insoluble matter usually separating out in an extremely fine state of subdivision.

A third object of precipitation is for *its value in chemical testing*. Practically the entire scheme of analytic chemistry (Chapter LIV) is based on the separation of compounds of the various elements from solution by the addition of an appropriate precipitant.

Operation.—As mentioned above, precipitation can be accomplished by either physical or chemical means, although by far the greater number of precipitates used in pharmacy and chemistry are produced by chemical means. Among the physical means of precipitation is the use of *heat*, as shown by the precipitation of the egg albumen from the mixture by heating when the albumen coagulates, as explained in the preceding chapter.

Another physical form of precipitation is *by changing the nature of the solvent*. As mentioned in Chapter VII, a substance may freely dissolve in one solvent, but be insoluble in another, and in such cases the addition to the solution of the substance of the liquid in which it is insoluble usually effects the precipitation of the solid, provided always that the added liquid is freely miscible with the liquid which holds the salt in solution. A case of this kind is that of acacia, which will be precipitated from its aqueous solution on the addition of alcohol. This separation, it will be noted, is purely physical, and it differs from the precipitation of acacia from its aqueous solution by the addition of lead subacetate, in which case chemical change is effected.

Among the chemical means of precipitation it is possible to include the action of *light*. Even that precipitation is frequently considered as a physical means, but it is true that precipitation effected by light is brought about by the light changing the chemical character of the precipitated substance. One case where light produces precipitation is with the salts of silver. Almost every pharmacist has noted the precipitation occurring in solution of silver nitrate exposed to the light when the sides of the vessel become coated with a black substance, which is metallic silver, the light acting on silver nitrate, reducing it to the metallic form. The usual chemical method of precipitation, however, is *by adding a precipitant*, as mentioned above, and as illustrated in the manufacture of precipitated calcium carbonate from prepared chalk.

These two substances are chemically identical, the only difference being that prepared chalk—a natural product—is only slightly purified by the process of elutriation and trochiscation; hence is apt to contain more or less impurities, and it is freed from these impurities by the process of precipitation.

In converting the prepared chalk into calcium carbonate, five stages in the operation may be noted. The first is to get prepared chalk or the calcium part of it into solution, for it is through solution that a substance can be readily freed from impurities.

To effect this solution a chemical change is necessary; in other words, the insoluble calcium carbonate must be converted into a soluble salt of calcium, and the salt selected is calcium chloride. This calcium chloride is produced from the prepared chalk by the addition of hydrochloric acid, the reaction being:

$$CaCO_3 + 2HCl = CO_2 + H_2O + CaCl_2.$$

The calcium chloride solution so obtained is filtered to effect a separation of insoluble particles, and this filtration might be considered the second stage of the process. The third stage of the process is the real precipitation, which is accomplished by adding to the solution of calcium chloride the precipitant, which is a solution of any soluble carbonate, and for practical purposes sodium carbonate is always used, the reaction at this stage being:

$$CaCl_2 + Na_2CO_3 = 2NaCl + CaCO_3.$$

It will be seen that, besides calcium carbonate (precipitated chalk), sodium chloride is formed, and the moist precipitated carbonate is wet—not with pure water, but with a solution of salt. If we dry the precipitate just as it separates from the liquid of which it was once a part, we get a product contaminated with salt, but if we wash it, the sodium chloride dissolves, leaving behind pure calcium carbonate moistened only with water.

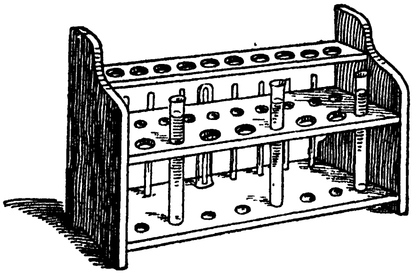


Fig. 167.—Test tubes in rack.

Therefore, we wash the moist precipitate, this constituting the fourth stage in the process of precipitation. Lastly, the moist precipitate must be dried, which constitutes the fifth and last stage of the process.

Apparatus used in precipitation by chemical means consist of a chemical flask or evaporating dish in which the insoluble substance is made into the soluble form, the funnel and filter by means of which the solution is rendered clear, the jar or dish in which the filtered solution is mixed with the precipitant, and where the precipitate is allowed to collect, a strainer or a plain filter in which the precipitate is collected and washed, and, lastly, a drying closet or other means of desiccation by which the moist precipitate is dried. All these pieces of apparatus have been considered except the precipitation jars; these consist either of tall cylinders or of beakers, both of which were illustrated under Decantation (Figs. 138, 139). The precipitating jar is of glass, made tall in order to effect the complete separation of the precipitate, thus facilitating decantation; the beaker is a vessel of thin glass so annealed as to stand heating.

For precipitation in chemical testing, test tubes are usually employed. These consist of narrow cylinders of glass, 5 or 6 inches long, with round bottoms (Fig. 167), while in quantitative analysis the precipitates are carefully collected in a beaker, as explained under Decantation.

The appearance of the freshly separated precipitate is described by appropriate adjectives, most of which are self-explanatory. Thus, we say that silver chloride is *curdy;* ammonio-magnesium phosphate is *crystalline;* aluminum hydroxide is *gelatinous;* coagulated albumin is *flocculent,* and magnesium phosphate is *granular.*

To these Bancroft adds 3 more types; colloidal (evidently a magma); jelly-like, which differs from gelatinous in the fact that the liquid phase is less prominent; and fluid, such as the separation of phenol when sodium phenolate is treated with acid.

Sometimes, when a precipitate is light and occupies considerable space, it is said to be *bulky.* A *magma* is a form of thick, tenacious precipitate, such as is formed by magnesium hydroxide in the official magma of magnesia.

In explaining a test, mere mention of the precipitant is not sufficient, but the color and character of the precipitate formed should be included in the answer. Thus, if asked the test for sulfuric acid or a sulfate, it is scarcely complete to answer "barium chloride," but such a question should be answered: "Barium chloride gives a white precipitate, insoluble in nitric and hydrochloric acid." The last part of this answer, while seemingly superfluous at first glance, is necessary, inasmuch as barium chloride forms white precipitates with several other acids, but it is only in the case of sulfuric acid and sulfates that the precipitate is insoluble, as mentioned.

In some cases the same substance can be precipitated in a light, flocculent form or in a heavy, granular form, giving rise to the distinction between *light* and *heavy precipitates.* These result entirely from the method of manipulation. If, in precipitating the substance, the solutions are dilute and cold, a light precipitate is usually formed, whereas if the two substances are mixed in hot concentrated solution, a heavy precipitate is formed. An official illustration of these two forms of the same substance is shown in magnesium oxide, U.S.P., and heavy magnesium oxide, these being produced by the calcination of light magnesium carbonate and of heavy magnesium carbonate respectively, the light being precipitated from dilute solutions and the heavy from concentrated solutions.

Cocking points out that 100 Gm. of bismuth subnitrate occupies a space of 50 to 75 cc.; that 100 Gm. of heavy magnesia measures 120 to 200 cc.; and that 100 Gm. of light magnesia measures 400 to 670 cc.

CRYSTALLIZATION

Crystallization is the process of separating substances in forms possessing definite geometric angles. Such substances are called "*crystalline*" while substances which cannot be made to form definite geometric angles are said to be "*amorphous,*" which some physical chemists consider as undercooled liquids. Among the latter are some substances which are sometimes erroneously considered crystalline, as, for example, the scale salts of iron.

In considering crystallization the first aim is to get an idea of what a crystal is. A crystal is a solid whose faces form definite angles, a body which can be measured according to the rules of geometry. Geometry is that portion of mathematics which deals with the measurement of surfaces and angles. Angles are formed where surfaces meet and vary in size, being measured by their relation to the circle. Thus, were a right angle cut from a circular disk from center to edge, it would remove one quarter of the circle. A circle in geometry is divided into 360 parts, called degrees, and since the right angle is one quarter the circle, its measurement is said to be 90 degrees. An angle of 60 degrees is but one sixth the circle, hence is sharper than a right angle.

An angle means what we usually call a corner—a space inclosed by the intersection of two straight lines. We have instruments whereby these angles may be measured, and the measurement of the various angles forms a part of the sciences of geometry and trigonometry. Among the practical applications of these sciences may be mentioned surveying and measurement of crystals.

Crystals are specially interesting as definite geometric forms assumed of themselves without outside aid. It is an easy matter for a skilled sculptor to hew a definite geometric form, but remember that a crystal form depends on no human aid. The substance composing the crystal groups its particles into the shape ordained for it from the beginning, and every perfect crystal of the same substance, be it large or small, has exactly the same form. Then, too, all substances do not crystallize with the same angles. One for ages has been crystallizing in a certain form, while one of its neighbors during the same period has produced numberless crystals all alike, but each of shape different from the substance first spoken of. In this way we have in the study of crystals an excellent method of distinguishing different chemical substances, and so large is the scope of the work that study of crystals is now classed as an independent science.

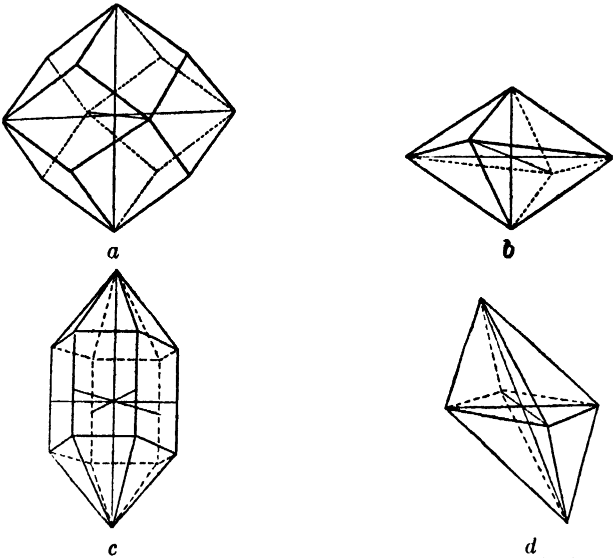


Fig. 168 —Crystal forms· *a*, dodecahedron; *b*, quadratic octahedron; *c*, hexagonal prism; *d*, double oblique octahedron (Holland).

In studying the crystal the crystallographer distinguishes four different parts of a crystal, the most important of which are the *angles* described above, an angle being the measurement of the conjunction of two *faces*, such conjunction being called the *edge*. These terms will best be understood by a study of Fig. 168, which also shows the fourth characteristic of the crystal, the *axes*, these being imaginary lines so drawn through the crystal that they intersect at its center. Each crystal has its peculiarities of faces, axes, and angles, and, therefore, all substances in crystalline form are grouped by crystallographers into various crystal systems, the main divisions being as follows:

Number of Axes		Length of Axes	Angle of Intersection
Regular	3	All equal.	All right angles.
Tetragonal	3	Two equal, 1 different.	All right angles.
Rhombic	3	All unequal.	All right angles.
Hexagonal	4	Three equal, 1 different.	Three at angle of 60 degrees, the fourth at right angle.
Monoclinic	3	All unequal.	Two oblique, the third at right angle.
Triclinic	3	All unequal.	All oblique.

Bragg studying x-ray photographs of crystals found that such photographs show that crystals have characteristic lattice structures. From these "crystal lattices" he and other investigators have been able to explain the exact arrangement of the atoms within the crystal.

The subject of crystallography is beyond the scope of the average pharmacist, its chief value being as an adjunct to the science of mineralogy; therefore, the rest of this chapter will be devoted to the pharmaceutic consideration of crystallization, and those desiring further information on the science of crystallography are referred to standard books on the subject. This is following the lead of the Pharmacopœia, which rarely mentions the scientific classification of crystals, contenting itself with the rather superficial general terms applied to crystals, such as saying that the crystal is "prismatic" (in shape of a prism), "tubular" (somewhat round like a cylinder), "acicular" (needle-shaped), etc.

In some cases mineralogists find half-crystals; in other words, the ideal crystal is split down its length. Such crystal splitting is called *cleavage*.

Isomorphism.—Substances which crystallize into the same form are said to be *isomorphous;* and, through the investigation of Mitscherlich, has been evolved the interesting theory that isomorphous bodies usually possess closely allied chemical composition. Thus magnesium sulfate, $MgSO_4.7H_2O$ and zinc sulfate $ZnSO_4.7H_2O$ are found to be isomorphous. In the same way the alums all crystallize in the same form.

Measurement of Crystals.—As mentioned above, crystallography is the study and classification of crystals chiefly according to the angle intersection, the measurement being made by the instrument called *goniometer*. There are a number of types of goniometers and detailed descriptions of these are clearly beyond the limits of this work.

Objects of Crystallization.—The pharmacist's consideration of crystallization is limited almost entirely to the production of crystals, and, therefore, the view of the pharmacist as to crystals is quite different from that of the crystallographer, the latter busying himself with the examination of the finished and usually native crystal, while the aim of the druggist is the production of a handsome crystal without special reference to the exactness of the angles. He produces a substance in crystalline form, merely to obtain them in a higher degree of purity, and to this he adds the esthetic consideration that a perfect crystal is the most beautiful form in which a chemical can be produced.

For practical reasons, however, the pharmacist usually prefers his chemicals in the form of granular crystals, rather than a large and perfect sample, the former being more readily soluble.

Production of Crystals.—The several ways in which crystals are produced are given place in order to their relative importance:

First, by cooling a hot saturated solution. This is the usual method of producing crystals in chemical manufacture, and the process can be readily understood by one who has studied the preceding chapter on Solution. Therein it was noted that a substance is usually more soluble in hot water than in cold; furthermore, that from this hot solution, on standing, will be deposited the excess of the substance.

Thus, as cited on p. 467, 100 cc. of boiling water will dissolve nine times as much potassium chlorate as will 100 cc. of water at 25° C., and when the temperature of this heated solution is reduced to 25° C., the 80 per cent excess will separate out, and, indeed, in the form of crystals, since the body is crystallizable. Such is the usual method of making crystals, the substance being dissolved in hot water, the hot saturated solution filtered through paper, the filtrate allowed to stand in an appropriate dish, usually for twenty-four hours, when the liquid is separated from the crystals which are then removed from the dish and dried.

Two technical terms are used in connection with this process. The saturated solution above the crystals in which the substance has formerly been dissolved is called the *mother liquor*, and again, in some cases of crystallizing this way a solution is concentrated by evaporating until a thin scum of crystals forms across the surface of the liquid, and this layer is called the *pellicle.*

Apparatus.—The apparatus used in this operation are the indispensable funnel and filter and the dish in which the crystals are collected. For small operations no better dish can be found than the ordinary pint evaporating dish. Glass beakers are sometimes used, but should be employed only for the collection of minute quantities, and when the crystals are not particularly large and strong as in the latter case the removal of the crystals from the sides of the vessel is liable to result in fracture of the glass. In all operations of crystallization crystals will separate out more readily if the interior of the dish is rough, although this detail is valued chiefly in crystallizing large quantities, for which purpose nothing is better than the ordinary earthenware crocks. The roughness of the vessel seems to attract the formation of crystals, the same way as does the introduction into the liquid of bits of glass or tightly stretched twine.

These extraneous aids to crystallization are called *nuclei*, and a familiar illustration of nuclei is the use of string on which rock candy crystallizes. The finished crystal must be drained from its mother liquor, and this is usually accomplished by throwing the wet crystal mass on a strainer, or, in the case of smaller quantities, on a filter, and allowing it to drain. The excess of the liquid is then removed by placing the crystals between sheets of filter paper, or, in the event of the substance being of a caustic nature, such as chromic acid, porous plates of unglazed earthenware are used.

In modern chemical manufacturing, special crystallization apparatus is now available. This type of apparatus is devised to promote the continuous growth of crystals of uniform size. The operating factors producing this result are regulation of temperature, of agitation of the solution and of the humidity of the atmosphere and also the mechanical introduction of seed crystals (or nuclei).

Second, by the gradual evaporation of a solution. This consists of a modification of the foregoing, the crystallizing solvent being in this case alcohol, ether, chloroform, or some other volatile liquid. In such cases the chemical (usually of plant origin) is dissolved in the smallest possible quantity of the liquid, the solution filtered into an evaporating dish and allowed to stand, when, due to the gradual vaporization of the solvent, the crystals slowly form in the bottom of the dish. In such case the crystals should be removed before the solvent has completely dissipated, in order that the impurities may be removed in the residual solvent.

Third, sublimation. Some chemicals, on subliming, solidify in the form of crystals. Such is particularly the case with benzoic acid, and this gives the method employed in the manufacture of this chemical from its natural source, the official benzoin. The drug is coarsely powdered, mixed with sand, and placed in a dish which is covered with a piece of cheesecloth. Over the dish is placed a cone of paper, and the entire apparatus is placed on a sand bath and heated at a temperature not exceeding 110° C. From the benzoin the benzoic acid is liberated in vapor form and rises within the cone, and is condensed by the lower temperature of the surrounding air in the form of beautiful crystals. (See p. 126.)

Fourth, by fusion and partial cooling. This method of crystallizing is of little value to pharmacists. One frequently cited application is the preparation of one form of sulfur crystals. In this operation a considerable quantity of the substance, say 200 Gm., is placed in a Hessian crucible and brought to a state of fusion. As the pellicle forms on the surface of the cooling mass a hole is punched through, and the remaining liquid carefully poured out. On completely removing the pellicle it will be found that the sulfur has deposited in the form of monoclinic crystals. In a similar manner Moissan prepared diamonds by melting iron and dissolving graphite therein, and allowing the mass to solidify, under great pressure, by plunging the white-hot mass into cold water. The solid mass is then treated with hydrochloric acid, which dissolves out the iron, when it is found that part of the graphite is converted into the crystalline form, diamonds, although the crystals are too small to possess commercial value. Perhaps Moissan's method is more properly considered as a case of deposition from saturated solution, as in truth the graphite is dissolved in the molten iron and is caused to separate out in crystalline form before the solvent has solidified.

Fifth, by effecting change in the character of the solvent. As mentioned under Solution, some substances are soluble in one solvent and insoluble in another. For example, sugar will dissolve freely in water and sparingly in alcohol. In this case, if to the concentrated solution of sugar is added alcohol in sufficient quantity, the sugar will separate out and, indeed, in the form of crystals. This method is used in effecting crystallization in many chemical operations, although its use in pharmacy is comparatively limited.

Sixth, by the electric current. This method is totally foreign to crystallization in pharmacy, and can be dismissed with the statement that handsome crystals of gold metal have been obtained by passing low currents of electricity through solutions of metal for long periods of time.

LABORATORY EXERCISES

CRYSTALLINE SODIUM SULFATE

Dissolve 50 Gm. sodium sulfate in 20 cc. warm water (not boiling) in pint flask, and filter into beaker glass. Let stand, and note sudden formation of crystals with evolution of some heat. Let stand until next day, and then collect crystals on plain filter and dry. The mother liquor which drains off may be evaporated some and may yield another batch of crystals, though not so fine nor so pure as the first.

Remarks.—The sudden formation of crystals occurs only when conditions are just right. (See p. 492.)

Filtration.—In all cases where filtration is for the purpose of clearing a liquid, a plaited filter is used. In case the solid part—be it in the form of granules, crystals, or precipitates—is wanted, plain filters are employed. (See p. 153.) Whenever aqueous liquids are to be filtered, the filter paper should be first wet with water.

CRYSTALLINE FERROUS SULFATE

Put 25 Gm. copperas in pint flask, and add thereto 25 cc. water and 5 cc. diluted sulfuric acid and a pinch of card teeth, and dissolve with gentle heat. Filter into beaker, and put in a pinch of card teeth and let stand (say one to three days) until good "crop" of crystals are obtained. Collect these on plain filter and dry.

Remarks.—This process resembles making granulated ferrous sulfate, for remember that granules are merely minute crystals. (See p. 174.)

Card teeth are added to filtered liquid to keep the crystallizing ferrous sulfate from being oxidized to ferric sulfate. They should be carefully removed from the finished crystals.

The *mother liquor* may be concentrated, when more, but poorer, crystals are obtained.

"ROCK CANDY"

Dissolve 25 Gm. sugar in 10 cc. water by means of gentle heat in Erlenmeyer flash; transfer, without filtering, into test tube, stick a glass rod or piece of twine therein, and let stand several days. The sugar will crystallize on sides of tube and on rod in large crystals.

Remarks.—The sugar solution (syrup) is too thick to filter. Rock candy is made commercially by pouring such a thick syrup into wooden vats containing frames strung with cord, and the sugar in crystallizing deposits on the cords, making the rock candy in strings. The cord acts as a nucleus. (See p. 170.)

Water of Crystallization.—In the case of crystallization produced by a separation from a solution, the solvent very frequently plays a rôle in the composition of the deposited crystal, although in some cases the crystal separates from the solution without combining with any of the solvent. The latter is usually the case when some solvent other than water is employed but sometimes, in separating from aqueous solution, some chemicals form crystals that are water free. If water combines with the separating crystal, as is usually the case in aqueous crystallization, it is designated as "*water of crystallization,*" and if alcohol combines with the chemical in the same way, it is called "*alcohol of crystallization,*" and in similar manner we find some crystals contain "ether" or "chloroform" or "acetic ether of crystallization," if these solvents have been employed in the process of making crystals. The last four cases are not usual, however, so our attention need be devoted to the water of crystallization.

By "water of crystallization" is meant water that is combined in some loose chemical way with the chemical of which the crystal is composed, and it does not mean the water adhering to a moist crystal. Thus, 47 per cent of a perfectly dry crystal of alum consists of this water of crystallization.

The determination of this water of crystallization is a very simple operation, all that is necessary being to heat a weighed quantity of crystals, first, on a water bath, when it will be noticed the crystals liquefy, and then on a sand bath, when the steam arising from the liquefied mass proves the presence of water. The heat being continued for a sufficient length of time, all the water will be removed, and a dried mass, known as the "exsiccated" salt, remains.

In the case of alum, 100 Gm. of the crystals dried with proper heat will leave but 53 Gm. of the exsiccated alum, showing that 47 per cent of same is water. The amount of water of crystallization found in a given chemical is exactly the same for all perfect samples, and a study of the question has shown that the quantity of water in a crystal is in molecular proportion to the quantity of the substance, thus permitting the numeric expression of the amount of water in the chemical formula of the compound. (See p. 400.)

In this case, when we give the formula of sodium sulfate, $Na_2SO_4.10H_2O$, we can deduce therefrom the molecular weight, and are brought to the conclusion that in every 278 Gm. of crystalline sodium sulfate there are 180 Gm. of water.

We can deduce in the same way from the chemical formula of potassium alum, $KAl(SO_4)_2.12H_2O$, that this contains 47 per cent of water of crystallization.

The term "water of crystallization" is gradually becoming obsolete, and instead we speak of the body containing such water as "hydrated." Thus, $Na_2CO_3.10H_2O$, is now called dekahydrated sodium carbonate, while the official form, $Na_2CO_3.H_2O$, is called monohydrated sodium carbonate, and this term constitutes the pharmacopœial name of this salt. Recently Barker and others have presented interesting explanations as to how the molecules of water of hydration are attached to the crystalline chemical. (See Bibliography, p. 178.)

Interstitial Water.—Among the chemicals which separate in crystal form from aqueous solution, without the absorption of water of crystallization, the best known example is common salt. This separates in handsome masses of cubical crystals, and, in separating, it very frequently mechanically encloses certain quantities of water which must be clearly differentiated from water of crystallization, because retained in a purely mechanical manner. Such water, which gathers in the interstices found in a mass of crystals, is called "*interstitial water.*" On heating a substance containing interstitial water the latter is converted into a steam which, on expanding, tears the crystal mass asunder with a crackling sound. This phenomenon, called *decrepitation,* is different from the deflagration of potassium nitrate, which is due to the liberation of oxygen.

Efflorescence and Deliquescence.—The crystals of some substances, sodium phosphate, for example, part so readily with water of crystallization that even at ordinary temperature the latter dissipates, causing the crystal to fall into a white powder. This loss of water of crystallization at ordinary temperatures is the phenomenon termed *efflorescence.* Special attention should be paid to the fact that an effloresced body means. one which has lost its water of crystallization and hence is stronger than the same body in the form of clear pure crystals. For this reason. in making a pharmaceutic preparation, care must be observed that, unless otherwise specified, the substance should be perfectly crystalline. If the effloresced salt is used in the same quantity as is directed for the crystalline, the finished preparation will be stronger than was intended.

Efflorescence, however, is not always loss of water of crystallization; thus when ammonium carbonate effloresces to ammonium bicarbonate, water of crystallization does not enter into the proposition (p. 507).

On the other hand, some crystalline substances have such affinity for water as to absorb same from the moist atmosphere, ultimately liquefying. Such substances are said to be "*deliquescent,*" and a notable example of such deliquescence is the case of potassium acetate, which should, therefore, never be dispensed in papers.

Certain solids absorb moisture from the air and become moist without liquefying. Such are called *hygroscopic.* Likewise certain liquids that absorb moisture from the air, such as glycerin, are said to be hygroscopic.

Efflorescence is now explained by physical chemists in terms of vapor tension of the hydrate. If kept in an open vessel, a hydrate having a higher vapor tension than that of water will lose its water of hydration and will therefore effloresce. Hydrates with a lower vapor tension will, on the other hand, remain unchanged. Thus, sodium sulfate, $Na_2SO_4.10H_2O$, at 9° C. has a vapor tension of 5.5 mm. Water at 9° C. has a vapor tension of 5 mm. Copper sulfate, $CuSO_4.5H_2O$, at 9° C., has a vapor tension of 2 mm.

In accordance with the principle just expressed, sodium sulfate crystals will effloresce while copper sulfate crystals are stable.

It has been found that deliquescence is a property of those substances, the solutions of which have a vapor pressure less than the vapor pressure of water vapor in air at the same temperature.

GRANULATION

Granulation is best defined as interrupted crystallization, while the operation of granulation is the process of heating a chemical substance with constant stirring until moisture is evaporated and a sabulous (coarse-grained) powder is produced. This definition, however, does not describe the manufacture of the so-called "granular effervescent salts."

In granulation a substance is prepared as in crystallization, by separation from a supersaturated solution. As mentioned under Crystallization, to secure large and handsome crystals by this method it is usual to leave the hot filtered liquid perfectly quiet, a stirring of the same producing small, ill-defined crystals. As such is exactly the object of granulation, in that operation the hot filtered solution is stirred and the separation of the crystals facilitated by evaporation of the substance from the liquid to a point where a very small quantity of solvent remains.

In granulating a substance, however, the evaporation should not be continued until all the liquid has disappeared, as a certain quantity of mother liquor is essential to remove soluble impurities by solution in the mother liquor.

Chemicals in granular form have of late years become quite popular, due to the more rapid solubility of same than the larger crystals, following the statement made under Solution that the latter is facilitated by comminution of the dissolving substance.

The term "granulation" is also applied to the mixtures which are prepared for making compressed tablets. Granulation must be effected in order to make the particles of the powder adhere when they are compressed. An ordinary powder will not compress into tablets which retain their shape and entity. It must be granulated to a certain extent in order to compress properly.

Apparatus.—In granulation the only apparatus needed are those required for crystallization from saturated solution, viz., flask in which the solution is made, apparatus for the filtration, evaporating dish, and glass stirring rod. The operation itself will best be understood by preparing Granulated Ferrous Sulfate, U.S.P. X.

LABORATORY EXERCISE

GRANULATED FERROUS SULFATE

Ferrous sulfate (copperas)	25 Gm.
Water	25 cc.
Diluted sulfuric acid	1.25 cc. (about 20 drops)
Card teeth	sufficient quantity
Alcohol	6 cc.

Place the ferrous sulfate in pint flask, add the water mixed with the acid, and lastly add a pinch of card teeth; warm gently on wire gauze over Bunsen burner until dissolved and the solution is a green color. Then filter through plaited filter into tared evaporating dish, and evaporate on sand bath until the liquid weighs 38 Gm. Then stir constantly until cool and throw mass on to funnel stopped with plug of absorbent cotton.

When the granules are completely drained of the mother liquid, pour the alcohol on the granules, and when this is drained, throw granules on filter paper and dry quickly without aid of heat.

Remarks.—This is practically the official process for making ferri sulfas granulatus, U.S.P. X. (See p. 565.)

Card teeth are pieces of bright iron wire, and a "pinch" means 2 to 5 Gm. When these are added to the solution in the presence of the acid, hydrogen is produced (note evolution), and this reduces any ferric sulfate present in the copperas to ferrous sulfate. This change is easily noted in the conversion of the brownish liquid to a pure green tint.

Tared dish means that the evaporating dish must first be weighed, and it is well to mark with lead pencil its weight on the outside of the dish. The liquid is then evaporated until dish and contents weigh the weight of the dish plus 38 Gm.

Sand Bath.—Any flat dish containing sand will do. (See p. 88.)

Collection of Granules.—Observe, instead of using a plain filter, the granules are collected on a plug of cotton in neck of funnel. This is to get the water off as quickly as possible, since green ferrous sulfate is very easily converted (at least partially) into red-brown ferric sulfate, especially when water is present.

Washing with alcohol is done to remove last traces of water, and the granules, when thrown on filter paper, are wet with alcohol and not with water. Alcohol being more volatile, the granules dry more quickly.

Dry at Low Heat.—No artificial heat must be used, else the green granules will change to a white powder—to the effloresced salt. As soon as dry, the granules should be bottled.

Granular salts are preferable to crystals in prescription work, because more easy to weigh and to dissolve. They usually save the necessity of powdering in a mortar.

Granular Effervescent Salts.—This class of preparations is totally different from the true granular salts, such as granulated ferrous sulfate, inasmuch as they are totally devoid of crystalline property, and are called "granulated," because consisting of the chemical in uniform and small particles. These will be discussed on page 327.

EXSICCATION

Exsiccation is the process of removing water of crystallization from a chemical by the use of strong heat. This process was foreshadowed on a preceding page (p. 172), so here it need only be added that the chief object of exsiccating a substance is to reduce its bulk. Thus, a crystal of alum weighing 10 Gm. contains but little less than 5 Gm. of water, and but little over 5 Gm. of the chemical itself, hence 5 Gm. of exsiccated alum represents approximately the same strength as about 10 Gm. of the crystal. In most operations the exsiccated salt has but little value over the crystalline, and perhaps is even less useful, as we usually employ chemicals in solution, and an exsiccated substance is usually more difficultly soluble than is the same substance in crystalline form. Therefore the chief use of exsiccated substances is for incorporation in pills, the size of which should be limited to 5 grains, and by use of 5 grains, of the exsiccated substance, we have about 10 grains of the same body in crystalline form.

It is necessary to point out that exsiccated alum has therapeutic value not possessed by the crystals (p. 548).

Apparatus.—The apparatus used in exsiccation consists of an evaporating dish, which should be tared, while the source of heat is usually a sand bath.

LABORATORY EXERCISES

EXSICCATED ALUM

Recipe.—Alum, in small pieces .... 20 Gm.
To make ... 11 Gm.

Place the alum in a tared shallow porcelain dish so as to form a thin layer, and heat it on a sand bath until it liquefies. Then continue the application of a moderate heat, with constant stirring, until aqueous vapor ceases to be disengaged, and a dry, white, porous mass weighing 11 Gm. is obtained. When cold, reduce the product to a fine powder, and preserve it in well-stoppered bottles.

Remarks on Process.—The recipe just given is similar to but not identical with that which was given in U.S.P. X.

Remarks.—Exsiccation is driving off water of crystallization from a crystal, and is here directed to be performed to show the student that a dry crystal does contain water, and that in large amounts.

On heating, the crystal liquefies by dissolving in the crystal water, and on further heating the water can be seen to vaporize, and if desired, the steam may be condensed on some cold surface. The loss of water is shown in the fact that 20 Gm. of crystal alum yields only 11 Gm. dried alum, representing a loss of 9 Gm. of water, or 45 per cent—$\frac{9}{20} \times 100 = 45$ per cent.

What is the actual percentage of water in $K_2Al_2(SO_4)_4.24H_2O$? Estimation by molecular weight (p. 400).

The dish must be tared and the mass heated until it weighs 11 Gm. plus weight of dish. Be sure to wipe all sand off dish before weighing, and also scrape all adhering alum from stirring rod and put into dish.

Stirring the tough mass is a matter of some difficulty. Best accomplished by holding a glass rod firmly down across top of dish and stirring with a smaller rod.

EXSICCATED FERROUS SULFATE

Recipe.—Ferrous sulfate, in coarse powder .... 20 Gm.

Allow the salt to effloresce at a temperature of about 40° C., in dry air, and then heat it in a porcelain dish, on a water bath, constantly stirring, until the product weighs about 13 Gm. Lastly, reduce the residue to a fine powder, and transfer it at once to perfectly dry, well-stoppered bottles.

Remarks on Process.—The recipe just given is similar to but not identical with that given in U.S.P. X.

Remarks.—*Effloresce,* losing water of crystallization at low temperatures (p. 173). Effloresce and finally exsiccate at low temperature, to avoid possible oxidation.

Note change from green crystals to a gray-white powder.

Note loss in weight from 20 to 13 Gm., a loss of 7 Gm. water, or 35 per cent ($\frac{7}{20} \times 100 = 35$).

This is not all the water in the crystals. Estimate by molecular weight, percentage in $FeSO_4.7H_2O$.

DIALYSIS

Dialysis or *osmosis* is a process whereby the crystalline portion of a mixture is separated from the noncrystalline by the passage of the former through a semipermeable membrane. The crystalline substance which passes through the membrane is called *crystalloid,* while the noncrystalline substances, usually of mucilaginous character, are called *colloids,* from the Greek *"kolla,"* meaning glue.

Diffusion, dialysis and osmosis are words used to indicate phenomena that are closely related. The term, diffusion, is usually applied to the mixing of adjacent layers of fluids or of gases, as obtains when alcohol is layered on water or when a heavy gas like carbon dioxide is passed into a cylinder containing air. Dialysis and osmosis, on the other hand, are used to indicate admixture by the passage of material through a porous membrane. Physical chemists now differentiate between dialysis and osmosis by applying the first term to the passage of the crystalloid solution into the water, and the word, osmosis, to the passage of water into the solution containing the crystalloid, for it is to be noted that both fluids pass through the membrane in opposite directions. This produces the phenomenon called *osmotic pressure* which is analogous to gaseous pressure and which like the pressure of gases can be expressed mathematically by equations in which one of the factors is the molecular weight of the substance studied. In fact, even as the molecular weight of gases can be deduced from their relative speed of diffusion, so from the osmotic pressure of a solution can the molecular weight of the solute be determined.

Although Speter states that dialysis through a bladder was described in a book printed in 1529, the modern use of this operation began with Graham in 1861. At the time of discovery it was thought it would be of great use in pharmacy and other arts. Experience, however, has shown that its value is largely theoretic; the study of plant and animal physiology proving that a large portion of the so-called "vital processes" going on in the living organism operates upon the principle of dialysis.

The apparatus used in pharmaceutical dialysis consists primarily of any porous membrane. For this purpose a bladder is usually employed, although parchment paper or unglazed earthenware may be used for the purpose.

The rest of the apparatus consists of two containers of glass. The membrane is attached to an open cylinder of glass or other suitable material, in such way as to serve as the bottom, and is made to rest upon the surface of water held in the second container, and upon the membrane is poured the liquid which is desired to be dialyzed (Fig. 169). This done, the crystalloids contained in the liquid on the dialyzer begin to pass through into the liquid below, whereas the noncrystallizable substance remains behind, thus affording a very simple method of separating the mixture of, say, sodium chloride and starch, the salt being crystalline, passing through the membrane, and the starch remaining behind.

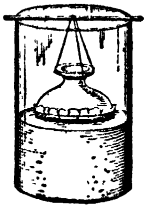


Fig. 169.—Dialyzer.

Objects.—As mentioned above, the most important object of dialysis is in the natural processes of animal and vegetable economy; some soluble solids pass from one cell to another by the process of dialysis. In the pharmaceutic application of dialysis a class of preparations, called "dialysates," were put upon the market. These are usually made by placing a decoction of plants on a dialyzer and evaporating the crystalloid liquid. The latter contains the crystalline alkaloid, whereas the residue left on the dialyzer consists of the usually inert colloidal substance. As examples of such preparations occasionally used may be mentioned dialyzed opium and dialyzed cinchona, but these preparations did not come up to first anticipations, and at the present time practically the only dialyzed preparation used to any extent in pharmacy is dialyzed iron, which is a colloidal preparation. (See p. 571.)

In chemistry dialysis is of some value in the separation of crystalloidal substances from obnoxious colloidal matter. This is particularly the case in toxicologic examinations, when searching for alkaloidal poisons the latter can be separated from the stomach contents by throwing the matter on a dialyzer and evaporating down the crystalloidal liquid. Even in this case, however, the application is somewhat limited because too slow, and other methods of separation are usually employed.

Colloids.—During the past fifteen years physical chemists have carefully studied that class of substances known as colloids and many puzzling points concerning the chemical behavior of these bodies have been now satisfactorily explained. Some ideas of colloids and of their application to modern pharmacy are given on page 408.

BIBLIOGRAPHY

Precipitation.—(General) Bancroft, Jl. Frank. Inst., 185, 1918, 373. (Silver) Roux, Jl. de ph. et ch., 27, 1893, 510. (Light and heavy precipitates) Cocking, Ph. Jl., 107, 1921, 226.

Crystallization.—(Crystal classification) Rogers, Am. Mineral, 13, 1928, 571, through C.A., 9. (Isomorphism) Tutton, Ph. Jl., 74, 1905, 894. (Efflorescence and deliquescence) Alexander Smith, Inorganic Chemistry; Findlay, Phase Rule, 1923; Boulanger and Urbain, Compt. rend., 155, 1913, 1246 and 1612. (Crystallization of carbon) Duncan, The Chemistry of Commerce, 1907, 105. (Crystal structure) Bragg, Ch. and

Dr., 88 (1916) 35 and Jl. Frank. Inst., 210, 1930, 9; Crehore, Phys. Rev., through C.A., 12, 1918, 117; Fedorov, C.A., 12, 1918, 9; Wyckoff, Jl. Frank. Inst., 195, 1923, 183, 349 and 531; Montillon and Badger, Jl. Ind. Eng. Ch., 19, 1927, 809; Pauling, Jl. Am. Ch. Soc., 51, 1929, 1015; Zachariasen, Z. Krist., through C.A., 23, 1929, 5371. (Crystal production) Moore, Jl. Am. Ch. Soc., 41, 1919, 1060; Steacie and Toole, Jl. Am. Ch. Soc., 51, 1929, 1134; Barker, Jl. Soc. Ch. Ind., 44, 1925, 19T; Gibbs, Jl. Inst. Ch. Eng., 8, 1930, 38. (Water of hydration) McLeod, Dr. Circ., 36, 1892, 224; Rakuzin, Bull. Soc. Chim., through C.A., 23, 1929, 1323.

Granulation.—(Ferrous sulfate) Trimble, A.Ph.A., 36, 1888, 140.

Dialysis.—Graham, Phil. Trans., 151, 1861, 183; Proctor and Redwood, Ph. Jl. [2], 3, 1862, 515; Procter, A.Ph.A., 12, 1864, 265; Speter, Ch. Zt., through Jl. Soc. Ch. Ind., 47, 1928, 1038. (Dialyzing membranes) Bigelow and Gemberling, Jl. Am. Ch. Soc., 29, 1907, 1576; Morse and Horn, Am. Ch. Jl., 26, 1901, 80. (Osmotic pressure) Van't Hoff, B., 27, 1894, 6; Stark, Science, 67, 1928, 556. (Uses) Graham, Ch. News, 4, 1861, 86.

CHAPTER X

EXTRACTION

UNDER the head of Extraction are grouped the processes in which the active and soluble constituents of a drug are separated from the inert insoluble portion by the use of an appropriate solvent. These processes comprise maceration and expression, percolation, digestion, infusion, decoction.

In order to understand the principle underlying the process of extraction it is necessary to appreciate the structure of the ordinary vegetable drug. Any drug representing a plant part is comprised of a collection of cells, lately living or long dead, each one of which possesses a wall of more or less thickness, this wall consisting of some variety of cellulose (possibly infiltrated with lignin), or tuberous, corky tissue. The cell wall is an insoluble thick envelop, scarcely permeable to liquid, while the active principles which we seek are generally found in the orifice encircled by the wall. To get the solvent in direct contact with the soluble constituents within the cell it is necessary that the cell wall be ruptured, hence in extraction we must first comminute the drug. The cells in some drugs are larger than others, hence some drugs are directed to be powdered more finely than others in various pharmaceutic processes, the aim of the pharmacopœia being to reduce the powder to a fineness sufficient to insure the breaking of every individual cell.

The quantity of cell wall, as compared to the amount of therapeutically active constituents, is usually many times greater. Thus, for example, in cinchona bark we find that but 5 per cent of the total amount is alkaloids, and no more than 30 per cent of the whole is soluble matter. Therefore the primitive method of administering the crude drug in powdered form meant the consumption, by the patient, of a large amount of not merely inert, but indigestible woody tissue, in order to get a small amount of medicament. To obviate the necessity of administering this large quantity of inert matter is the prime object of extraction, and in each case cited above it is accomplished by treating the drug with an appropriate solvent, and the removal, by solution, of the useful principles from the inert insoluble residue. Various extraction processes are also applied in obtaining active principles of animal glands and tissues such as thyroid extract, pituitary extract, liver extract, insulin, and others.

MACERATION

Maceration is the process of removing the active principles from a drug by allowing the latter to remain at room temperature in contact with the solvent several days, with frequent agitation.

Roughly stated, maceration consists of reducing the drug to appropriate fineness of powder, placing it in a suitable bottle, pouring on the solvent, which is called *menstruum* in all cases of extraction, and letting the mixture stand for a week, shaking at frequent intervals. The solution is then removed from the inert matter by filtration or straining, and the yield of filtrate increased by subjecting the residue to expression.

The process of maceration is a favorite method of extraction in most European countries. In America maceration is used only where percolation is precluded, and it is, therefore, limited to the few drugs the gummy or viscid character of which would cause a clogging of a percolator. The German Pharmacopœia directs maceration exclusively in the manufacture of tinctures, and even in this country some of the older pharmacists still cling to the process of maceration in the preparation of a large number of tinctures, the advantages they claim for maceration being, first, that the drug need not be powdered so finely as in the case of percolation, second, that the process requires less skill than does percolation, and hence requires less care in manipulation, and, third, that in the process of maceration there is less loss of alcoholic menstruum than in making the same preparation by percolation.

The latter is practically the only advantage possessed by maceration over percolation, the other questions not being worthy of attention of the intelligent and educated pharmacist.

In large quantities of a preparation made by maceration, say, gallon lots, the shaking of the bottle containing the drug and menstruum is a laborious task, and since the shaking is merely to bring all portions of the solvent in contact with the drug, and as the same result can be obtained by the process of circulatory solution (p. 144), this method can be employed in the maceration of tinctures, the ground drug being placed in a cloth bag and suspended directly below the surface of the solvent.

As mentioned above, the inert residue remaining after maceration (which is called the *marc*) is impregnated with the tincture itself and in filtering off a macerated tincture—say, of arnica—the residue on the filter is not wet with alcohol, but with full strength tincture. Hence, it can be seen that the process, even at its best, is wasteful; that the drug is never completely exhausted of its active principles, and the less care used, the more waste there is to the process. The waste is partly obviated by "squeezing the dregs," as we commonly say; by expressing the residue.

EXPRESSION

This is the process of removing the liquid from the moist mass by the use of pressure, one of the best pharmaceutical illustrations of the application of expression being in the removal of the remaining tincture from the marc.

Apparatus.—Many forms of presses have been devised, each adapted for some special phase of expression.

All forms of presses, with the exception of forcible straining apparatus and the Enterprise screw press, consist of two plates between which the substance is placed, and which are made to approach each other by means of lever, screw, or some other mechanical power.

Important in the process of expression is the straining of the expressed liquid through suitable cloth. We therefore, usually inclose the mass to be expressed in a bag of stout cloth (press cloth) before placing it in the press.

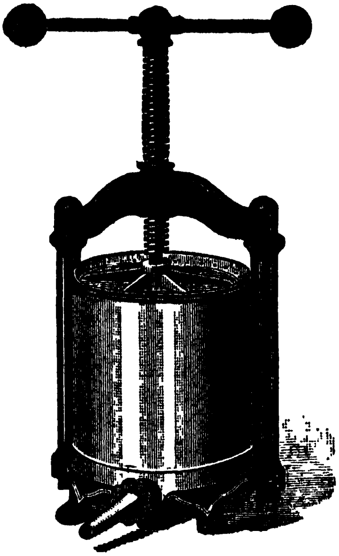


Fig. 170.—Tincture press.

Such press cloth (strong toweling will do) can be used directly for expression, as already explained under Forcible Straining (p. 151).

The *spiral twist press* is based on this principle, but is entirely useless in pharmacy, hence its bare mention will suffice.

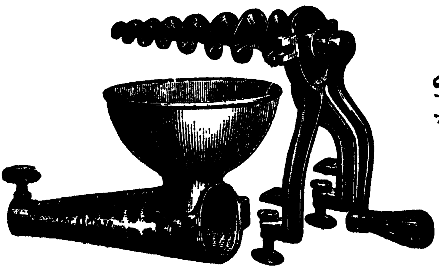


Fig. 171.—Enterprise press (opened).

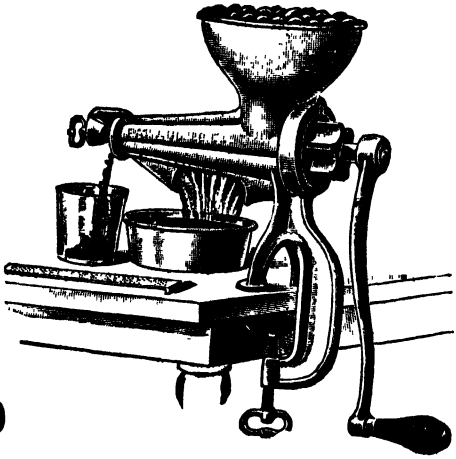


Fig. 172.—Enterprise press.

Other forms of presses of little pharmaceutic value, but used in other technical lines, are the *wedge press*, the *roller press*, which operates on the same principle as the roller clothes-wringer, and is seen in its form of highest perfection in the rollers used for expressing the juice from the sugar cane, and the *hand-lever press*, in which the upper plate is pressed down upon the lower plate by means of a lever.

In modern pharmacy expression is performed with the *screw press* or tincture press (Fig. 170), in which the moist mass is subjected to pressure between two steel plates, the upper one operating on a screw, such as is seen in the ordinary letter press. A very striking modification of the screw press is the *Enterprise press*, which will be best understood by an examination of Figs. 171 and 172. Of great value and increasing popularity is the *hydraulic press*, the only objection to which is its initial cost. This is constructed on that principle of hydrostatics which asserts that if a liquid be in communicating tubes—one larger than the other—any pressure on the surface of the liquid in the smaller tube will be exerted

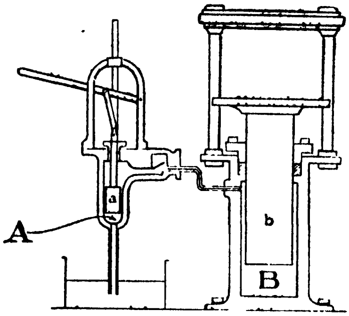


Fig. 173.—Hydraulic press (schematic).

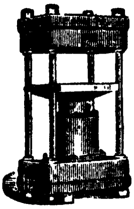


Fig. 174.—Hydraulic press.

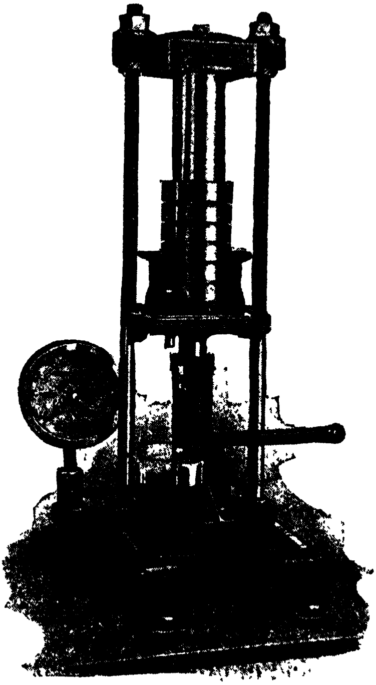


Fig. 175.—Carver laboratory press.

on the surface of the liquid in the larger tube in exact proportion to the relative size of the two tubes. This can be explained more clearly as illustrated in Fig. 173.

Suppose, in this sketch, that the area of the cylinder A is 1 square inch, and that of cylinder B is 10 square inches; then, if we exert a force of 1 pound on piston "*a*" we will get a force of 10 pounds on piston "*b*." By using a lever on piston "*a*" we can so multiply the force that a pressure of 10 pounds on the handle of the lever connected with piston "*a*" can readily exert the pressure of 1000 pounds on piston "*b*"; hence the great value of the hydraulic press, with which comparatively little power can be concentrated into enormous pressure.

Carver now markets a laboratory press 3 feet tall, weighing 115 pounds and exerting a pressure up to 10 tons (Fig. 175).

An interesting form of removal of liquid from a moist mass without the aid of a press is the operation of the centrifugal machine, in which case the moist mass is placed in a perforated cylinder, which revolves in a large cylinder with velocity great enough to cause practically all traces of the liquid to be thrown out of the inner into the outer cylinder (Fig. 176). By means of such a centrifugal press 200 or 300 pounds of moist sugar can be centrifuged to almost dryness in the space of five or ten minutes. A modern application of the centrifugal machinery, totally different from expression, is the well-known centrifugal sedimenter, for the precipitation of blood and of urinary sediment (Fig. 177).

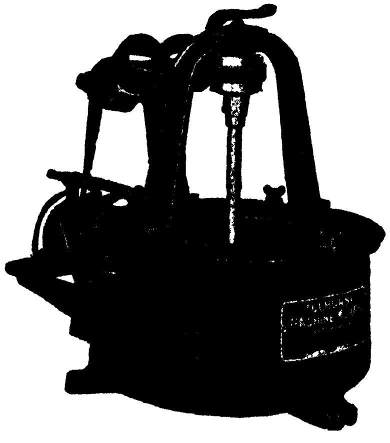


Fig. 176.—Tolhurst centrifuge.

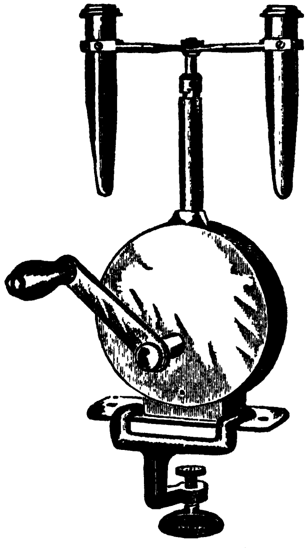


Fig. 177.—Urinary centrifuge.

DIGESTION, INFUSION AND DECOCTION

These three processes are types of maceration (or possibly percolation) with heated solvents.

Digestion in the ordinary pharmaceutic sense is maceration with warm water; that is, water heated below its boiling point. This is usually accomplished by placing the vessel containing the drug and the water in a warm place, such as the back of a stove or on a radiator. In certain cases of digestion, however, as in certain chemical practices, the material is digested with water or with some other solvent at high temperatures in an *autoclave*. This is a steel vessel (Fig. 178) with a cover that can be clamped on, in which the substance and the solvent can be heated much above the boiling point of the latter at ordinary pressure. In such an autoclave, under a pressure of 6 to 7 atmospheres (see p. 104) water can be heated to over 150° C.

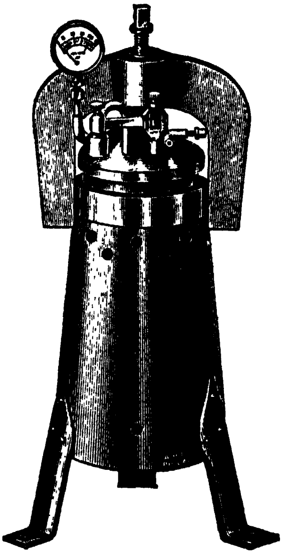


Fig. 178.—Autoclave.

Infusion and *Decoction* are described under the preparations bearing their names (pp. 237 and 238).

PERCOLATION

Percolation is the process of depriving a drug of its soluble constituents by passage of a solvent through the powder contained in a suitable vessel. The solvent in this case is called the *menstruum*, the vessel is called the *percolator*, and the solution of active principles emerging from the percolator is called the *percolate*.

History.—Lixiviation, the extraction of lye from ashes, has been used since ancient times: Rumford devised the plan of making coffee in the drip coffee pot in 1813; Johnson (1817) extracted cinchona in an apparatus like Rumford's; Real used a percolator press for removing the oil from almonds; Boullay (1833) and Robiquet (1835) introduced the method and it was directed for some preparations of the French Codex of that year; Procter and Duhamel first described the process in this country and it was employed in the Pharmacopœia of 1840, since which time it has been so much more popular in this country than in Europe that it can almost be considered an American process.

Principle of Operation.—Careful study of the definition of percolation will show that in the process advantage is taken of the attraction of gravitation, for it is hardly necessary to say that a liquid poured on top of a powder contained in a suitable utensil will gradually penetrate that powder in a downward direction, and if there is an orifice in the bottom of the vessel, the descending liquid will emerge from the vessel, being attracted by gravity toward the center of the earth. This downward force of gravitation is aided by another force, merely a modification of the former, namely, the weight of the column of liquid above the powder. Mention of the latter is made here merely because the downward force varies according to the height of the column of liquid, whereas the force of gravitation remains unchanged. If this combined action of gravitation was the only force coming into operation, the process would be a simple one. However, there is an opposing force which comes in to play while the process of percolation is in progress, namely, the upward force referred to as capillarity.

The term *capillarity* comes from the Latin term "*capilla*," meaning hair, because it was first observed that in every narrow, hairlike tube liquid was drawn up by the cohesive power of the walls of the tube, and, as already explained, to this same force is due the appearance of the meniscus (p. 58). All bodies possessing orifices more or less narrow have this property of drawing up liquids by their own cohesive force, and such is eminently the case with most vegetable drugs, since, as is mentioned above, they consist of a mass of cells, each cell consisting of a more or less minute orifice, surrounded by a cell wall. In other words, cells can be compared to long sealed tubes, and when the cells are broken by powdering, we have a vast mass of tubes, each possessing capillary attraction. This capillarity explains why a so-called porous substance, for example, a sponge, will absorb so much more water than a nonporous substance, such as sand.

To get back to percolation, besides the force of gravity and its modification, the pressure of the column of liquid above, forcing the solvent downward through the drug, we have at the same time capillarity of the cells of the drug attracting the menstruum in the opposite direction. The moment the solution commences to emerge from the vessel, the capillary attraction of the cells tends to keep the liquid within the substance; therefore, acting against the force of gravity. Experience shows that the capillary force of the drug is usually greater than the simple gravitating force of the earth, for unless the gravitating force of the earth is reinforced by the height of the column of liquid above the powder, the liquid ceases to drop from the percolator. As the liquid passes through the drug on its downward course it penetrates the interior of each cell (provided the substance is in fine enough powder) and removes from the same the soluble constituents. Passing from one series it penetrates the next tier of cells, and, taking up more active principles, such solution continues until the solvent is saturated with the soluble principles of the drug. When once a saturated solution, it mechanically passes through the rest of the drug, and finally emerges from the orifice of the bottom of the percolator, providing always that there is a sufficient column of the liquid to force it down. Its passage is followed by a fresh portion of the solvent, which passes through the same cells which it has formerly penetrated, removing the last vestiges of soluble matter, and finally emerging from the percolator also a saturated solution. In this way menstruum is continually poured on until the cells have been so completely exhausted of their soluble constituents that the final portion of the menstruum comes through devoid of color and taste, whereupon the drug is said to be *exhausted.*

The great advantage percolation possesses over maceration is in the fact that, by means of percolation, we are enabled to completely remove every trace of soluble matter from a drug, inasmuch as the saturated solvent does not remain in contact with the drug (if the menstruum column is maintained), but passes from it, being followed by a fresh portion of solvent, which removes the remainder of the soluble principle.

Apparatus.—The utensil in which the drug is packed is called a *percolator,* and consists of a suitable cylindric vessel of metal or glass, provided with an orifice at the bottom. In selecting percolators those of glass should be chosen when possible, metal percolators having the double disadvantage of being more easily attacked by acid or other substances which the menstruum or drug may contain and also the fact that their opacity prevents watching the operation. Of course, however, there are certain limits to the size of a glass percolator, the writer's experience being that the use of a glass percolator larger than 2 gallons is an expensive luxury, inasmuch as such are costly and are quite liable to break. Above 2 gallons, recourse was had to the galvanized iron percolator or the well tube percolator, in which the container is an earthenware crock.

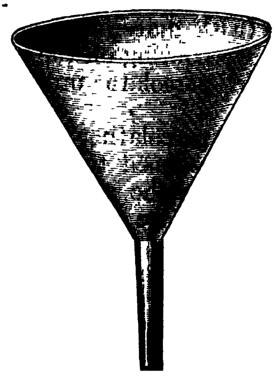


Fig. 179.—Conic percolator.

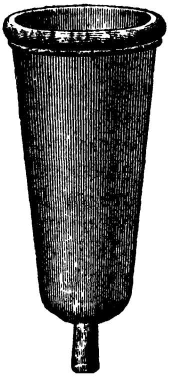


Fig. 180.—Tapering percolator.

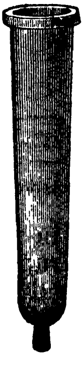


Fig. 181.—Oldberg percolator.

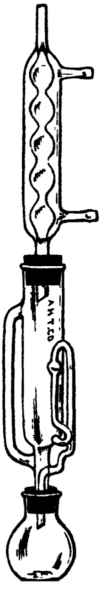


Fig. 182.—Soxhlet extraction apparatus.

Shape of Percolators.—The simplest form of percolator is the conic (Fig. 179), consisting of an ordinary chemical funnel. This, however, offers too great a width of surface for the menstruum, which, therefore, has a correspondingly smaller course to travel before emerging from the bottom of the percolator, and, therefore, the familiar tapering percolator came into use (Fig. 180). At the present time the Oldberg (or more properly Diehl) cylindric percolator (Fig. 181) is very popular, for by means of it we are able to exhaust a drug far more thoroughly than in either a tapering or a conic percolator, from the simple fact that each portion of menstruum has to travel through a larger amount of the drug before emerging from the percolator. A variety of percolator used exclusively in chemistry is the Soxhlet Extractor (Fig. 182). The Landsiedl modification of the Soxhlet is arranged with a set of special extracting thimbles, which permit the use of the apparatus for extraction of aqueous solutions with immiscible solvents.

The saturated solution, when emerging from the percolator, is called the *percolate,* and, of course, this must be collected in an appropriate vessel. For this purpose a wide-mouthed bottle, the receiving bottle, is usually employed. Elaborate forms of receiving bottle are on the market in which the graduations are engraved upon the glass. These, while presenting an elegant appearance, are scarcely necessary, as the pharmacist has many wide-mouthed bottles at his disposal, and he can usually graduate same by pouring in definite quantities of liquid from an accurate graduate, and marking amount by cutting with a file or on a strip of paper pasted along the length of the bottle (marking same with ink). The percolator must be supported on an appropriate stand, and for this purpose nothing can be better than the retort stand pictured in Fig. 86, it being always understood, however, that the glass percolator must never come in contact with the iron ring, being protected from the same by covering the ring with paper or cloth (Fig. 183).

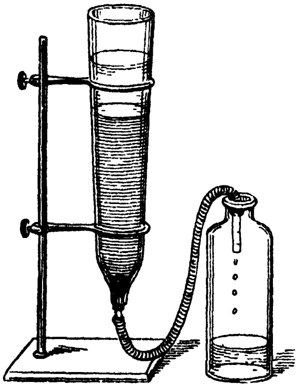


Fig. 183.—Correct percolation.

When large amounts of percolation are being carried on, special percolating stands have been devised; such, for example, as the Shinn percolating closet and the Remington percolating shelf.

Operation.—The process of percolation may be considered under the following headings: comminution of the drug; moistening the same; packing in percolator (with maceration either before or after packing); pouring on the menstruum and collecting percolate until exhausted.

Comminution.—Before percolating the drug it is essential that it be reduced to particles of more or less fineness, for the same reason that we comminute drugs before solution. As mentioned above, in percolation it is essential that the drug be ground sufficiently fine to rupture all the cells of which it is composed, and this degree of fineness is dependent upon the structure of the drug, those drugs having small cells calling for a finer degree of comminution than those in which the cells are large. Thus, ipecac must be powdered very finely, whereas in glycyrrhiza the cells are large and a coarse powder can be utilized. This explains why the Pharmacopœia directs various degrees of fineness for the powders used in percolation. Another point regarding comminution of the drug is the rapidity or completeness of exhaustion. Thus, in percolating fluidextracts it is usually desirable to exhaust the drug with less menstruum than in preparing tinctures from the same drug, and in order to do this the drug used in percolating a fluidextract is generally directed to be in finer powder than that used in making the tincture. The powdering of the drug is accomplished by those methods of comminution described in Chapter VI best serving the particular purpose, the main requirement being that the drug used in percolation be of uniform fineness.

Moistening of the Drug.—Before packing the drug in the percolator it is directed to be moistened with menstruum, this being done because, when the drug comes in contact with the menstruum, the compressed dried cells are swollen to their normal size, and if this swelling occurred within the percolator, it would cause sufficient expansion to cause a stoppage of the operation.

This moistening is accomplished by placing the drug in a suitable container, preferably of porcelain or stoneware, adding the required quantity of menstruum, and mixing it thoroughly with the drug by stirring with a wooden paddle. After being moistened it should be allowed to remain for half an hour in order to complete the swelling.

Packing of the Drug.—To receive this moistened powder a clean and absolutely dry percolator is prepared by placing in its neck a plug of absorbent cotton. Upon the plug of cotton, the moistened powder is poured into the percolator for the directed period of time, is then poured from the percolator into a suitable container and is then carefully packed in the percolator, the usual rule being to place in the percolator about one fourth at a time, and each fourth is firmly packed before the next portion is added. The packing is accomplished by means of a wooden plunger, and for this purpose a piece of wood will suffice, there being nothing better than a wooden potato masher. The packing of the drug is a matter of skill, and in order to do it successfully it is necessary to know the character of the drug and the menstruum. Drugs in finer powder are not, as a rule, packed so tightly as those of coarser powders, but the supreme test of the correct packing is the rapidity of the flow of the percolate. If the drug is packed too tightly, the percolate drops too slowly, and if too loosely, the percolate runs too rapidly to fairly exhaust the drug. In short, packing must be put down as chiefly a matter of experience. The nature of the menstruum also has an influence on the packing of the percolator. If the menstruum is pure alcohol, the drug can generally be packed more tightly than if it consists of water, and if glycerin is present in the menstruum, care should be taken not to pack the drug too tightly. It is hardly necessary to say that in packing the drug the pressure should be equal on all sides of the powder. If the drug on one side of the percolator is packed more loosely than on the other, it stands to reason that the menstruum will choose the easiest possible way and will run down the looser side, and, therefore, the drug will be incompletely exhausted.

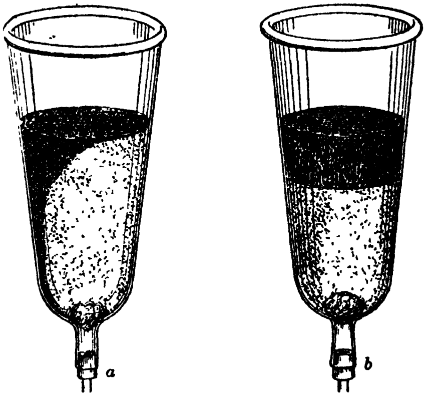


Fig 184 —*a*, Improper packing; *b*, proper packing.

All the drug being packed in the percolator, there is carefully placed above it a sheet of filter paper which is held in place by a glass weight, any unused glass stopper answering the purpose. The object of the paper is to prevent the disturbance of the powder when the menstruum is poured in, the force of the fall of the liquid being apt to cause the rising of the powder to the surface of the menstruum.

Instead of filter paper, the writer found very convenient disks of ordinary clean Manila cardboard, made from one of the many rejected pasteboard boxes found in every drug store. These disks, perforated by the point of a file, when just the size to fit snugly above the drug within the percolator, required no weight to keep them down.

Whether the drug has been packed evenly on all sides is shown by the descent of the first menstruum, which should go down in a perfectly even ring, as shown in Fig. 184, *b*.

After the drug is packed in the percolator and enough menstruum has been poured in to fully penetrate the drug and to begin dropping from the percolator, the lower orifice is closed and the drug is directed by the Pharmacopœia to macerate within the percolator for a period specified in the official recipe, after which time the percolation is begun.

Adding Menstruum.—The menstruum is, as mentioned above, the solvent used for extracting the active principles of the drug. The various menstrua directed by the Pharmacopœia for different drugs have been carefully selected with a view to using the particular solvent best adapted easily and speedily to remove the active principles of the drug under consideration. In some cases, however, the pharmacopœial committee has been guided by practical commercial considerations, the rule being to choose as menstruum the cheapest solvent that will fully answer the purpose. Understanding this fact, the pharmacist should carefully follow the pharmacopœial instructions, appreciating that when the United States Pharmacopœia directs strong alcohol, it is because a weaker alcoholic menstruum will not answer the purpose.

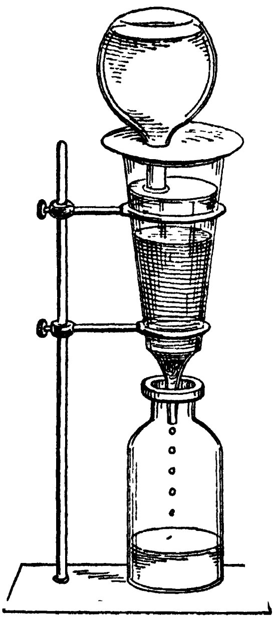


Fig. 185.—Continuous percolation.

Usually the menstrua used in percolation are of various mixtures of alcohol and water; occasionally glycerin is directed to be added to the menstruum, this usually in cases of drugs containing large quantities of tannin. In the same way ammonia water is added to the menstruum in preparations of licorice, and ammonia or other alkalis for drugs containing pectin, while acids are used in the menstrua for drugs containing volatile alkaloids, such as conium, ergot, etc.

Not all percolates are made with alcoholic menstrua; for example, some infusions are made by percolation of the drug with water—infusion of cinchona (U.S.P. 1890) with water plus aromatic sulfuric acid, and infusion of wild cherry (U.S.P. VIII) with cold water. Again, stronger white wine was used as a menstruum in the preparation of percolated wines of the pharmacopœia of 1890. Dilute acetic acid is used in those vinegars made by percolation, while oleoresins are made by percolating the drugs with ether or acetone.

The Percolation.—The proper menstruum is poured upon the filter paper above the powdered drug in the percolator, care being taken to pour it so as not to cause the floating of the paper. As the menstruum passes down through the drug, more is added to take its place, it being an unvaried rule that there should always be maintained a layer of menstruum above the surface of the drug, for, if the drug is exposed to the air, evaporation takes place from its surface, and fissures occur through which the menstruum added afterward will run, instead of through the entire surface of the drug. In order to keep a sufficient quantity of menstruum upon the surface of the drug, recourse is had to continuous percolation by inverting the menstruum bottle within the percolator in the same manner as suggested in continuous filtration (Fig. 185). The menstruum poured in and passing through the drug should emerge from the percolator slowly and steadily, the rapidity being dependent upon the quantity of the drug being manipulated, the character of the drug and the particular method employed.

The U.S.P. XI directs the rate of flow of percolate in each case in these terms: "percolate slowly," "percolate rapidly," or "percolate at a moderate rate." On the basis of a quantity of 1000 Gm. of drug these terms are defined as follows: "percolate slowly" means a rate not exceeding 1 cc. per minute; "percolate at a moderate rate" means a rate of 1 to 3 cc. per minute; and "percolate rapidly" means a rate of 3 to 5 cc. per minute. It is needless to say, however, that these standards must vary when large volumes of tinctures or fluidextracts are prepared.

In most operations in retail pharmacy, however, in which we deal with 200 to 1000 cc. of menstruum, the speed given above may be maintained, and a skilful operator aims to so pack his drug as regularly to attain this speed, and after some practice usually learns the art. In order, however, to insure the speed of percolation directed, the Pharmacopœia directs that the lower orifice of the percolator be closed with a cork through the perforation of which passes a glass tube which is fitted with a rubber tube at least as long as the percolator and terminating with a second glass tube bent in the form of a "V." When the rubber tube is raised so that the outlet is above the surface of the menstruum in the percolator, it follows that no liquid will run out, whereas if it is lowered to its greatest depth, the liquid will run out very rapidly, and, by raising or lowering the tube to its greatest height or greatest depth, the rapidity of the percolation can be regulated to a nicety. (See Fig. 183.) If it is desired to close the tube completely, a pinch-cock (p. 116) can be used, although if the tube is of sufficient length, this is scarcely necessary.

In practice, the rubber tubing is not so convenient as it seems at first blush, as the several joints of the cork, the glass tube, and the rubber tube fittings are apt to leak unless very carefully prepared, making an unsightly and dirty process. If, therefore, the percolating tube is used, care should always be taken *before percolation* to see that the cork and rubber tubes do not leak by pouring water into the empty percolator, raising the tube to its greatest height, and allowing it to stand in that way for some time.

Many pharmacists omit the use of the rubber tube, substituting therefor an ordinary cork with notches in the side, which do not extend through the entire length. If the percolation is desired to be stopped, the cork is pushed up into the neck beyond the notch, when an absolutely watertight fitting occurs. When the flow is desired, the cork is loosened so as to allow a part of the notch to be beyond the neck of the percolator, leaving a tiny orifice through which the liquid can be dropped. This scheme is usually satisfactory, although the tightening and loosening of the cork during the process of percolation are apt to be untidy. Far better, therefore, is the use of a metal sprinkler top, such as is used for tooth-wash bottles provided the percolate is free from acid or other substances that might act upon the metal.

Finishing Percolation.—In making preparations by percolation it is generally intended that the percolation be continued until the drug is exhausted, the word meaning in this case the removal from the drug of all its soluble constituents. There are several ways of proving the practical exhaustion of a drug, for, in the operation, it is usually unnecessary to carry on percolation to the extreme point of removing every particle of soluble matter. If the drug is a bitter one, we generally say it is exhausted when the percolate comes through no longer bitter, even though it may be still impregnated with some of the coloring matter residing in the drug, the latter being more tenacious and persistent of removal. In some cases the bitterness is so great that a large amount of menstruum will be necessary before every trace of bitterness is removed. An example of this is quassia, in which case we generally consider the drug exhausted when the percolate is almost free from bitterness.

Tannin-bearing drugs are usually percolated until the percolate is free from astringency, whereas in odorous drugs the absence of odor from the percolate announces exhaustion.

The residue left after percolation or maceration is called the *marc*, and in both percolation and maceration it retains a considerable amount of moisture. As mentioned under Maceration, in the latter case the moist liquid is the finished full strength tincture, and this marc should always be expressed, else the yield of tincture will be lessened. In percolation the marc is moist with the menstruum, hence there is no loss so far as finished tincture is concerned, but the loss of menstruum is excessive. It, therefore, behooves the economic pharmacist to recover the alcohol from this marc, which can be done by the process of steam distillation. During the writer's experience in practical pharmacy it was his custom to keep on hand a number of half-gallon wide-mouthed candy jars, securely corked, and in these he threw the successive batches of marc at the end of every percolation. When sufficient quantity had accumulated in these bottles, his steam distillation apparatus was fitted up, the tube from the boiler fitted into the candy bottle, and steam passed through and the vapors collected. The yield of alcoholic distillate more than paid for the fuel and time employed.

This process is found more convenient and efficacious than the ordinary method of pouring water on the drug, and thus forcing the menstruum out, as in the latter case the addition of water to the starchy matter remaining in the marc is apt to cause a swelling of the drug and subsequent clogging of the percolator.

During the past decade, the principles of percolation have been carefully studied by Husa and his associates. His findings, based upon the extraction of belladonna root, yellow cinchona, and nux vomica, are as follows:

1. Extended maceration of the drug before percolation is unnecessary. Fifteen minutes of maceration is as effective as twenty-four hours.
2. Maceration (for more than fifteen minutes) before packing the drug in the percolator is unnecessary.
3. The amount of moistening liquid used prior to packing must be kept low.

Hatcher and Lichtman and also Briedel and Barel report that preliminary maceration is unnecessary.

Modified Percolators.—Under Distillation and Comminution we found that ingenuity had devised many special apparatus for carrying on both operations, and the same also holds good in regard to percolation.

Chief among these improved forms of percolators must be mentioned the Squibb's well tube percolator (Fig. 186), which is primarily designed for the percolation of large quantities of drug. As mentioned above, under the consideration of the percolator itself, glass or earthenware percolators larger than 2 gallons are inconvenient to handle. Therefore, in large manufacturing establishments recourse is had to either huge metal percolators or to percolators made of wood. Metal percolators are not advisable, for acids from the drug or menstruum may attack the metal and render the product liable to contamination by metallic contact, while wooden percolators, even if unobjectionable from the standpoint of contamination, becoming saturated from contact with an alcoholic solution of a certain drug, can be used for the percolation of that drug alone, and, therefore, in their use a separate percolator must be provided for each drug desired to be percolated. The chief cause of the frailty of glass or earthenware percolators is their funnel form, which also increases their cost. Earthenware crocks with flat bottoms can be obtained of almost any size and for prices comparatively low, and, possessing a firm foundation, are very durable; hence the use of same in percolation was suggested to the fertile mind of Dr. Squibb, whose experiments brought forth the well tube percolator, which consists of an earthenware crock with the inside bottom fitted with a sheet of felt for filtering purposes, and the drug packed therein around a large glass tube. If, upon the drug so packed, menstruum is poured, it percolates through to the felt, then rises in the interior of the central glass tube to practically the same height as it is on the outside, following the well-known law of a liquid seeking its own level.

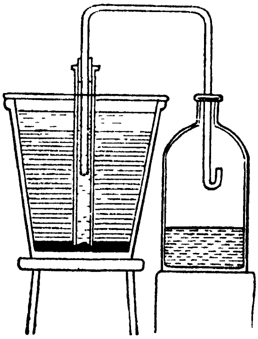


Fig. 186.—Squibb's well tube percolator

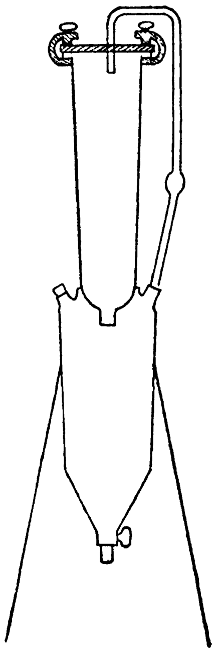


Fig. 187.—Economic percolator.

Now, if in this tube is placed a syphon, the liquid within the well tube can be drawn off, and if a sufficient quantity of menstruum is kept on drug outside the well tube, a constant level can be maintained in the well tube ready to be drawn off through the syphon. In order to maintain a constant flow from the syphon its lower end must be bent up as shown in cut, making the orifice at least $^{3}/_{4}$ inch higher than the orifice of the short arm. If this precaution is not taken, the liquid in the well tube is syphoned off more rapidly than it percolates, emptying the syphon immediately (Fig. 186).

Among the other forms of modified percolators are the various pressure percolators, such as Rosewater's and Berry's, both of these being based on the principle of the Real percolating press. With these, drugs can be percolated very rapidly and quite thoroughly.

Volatile Liquid Percolators.—In the manufacture of oleoresins by percolation with ether care must be taken to avoid undue evaporation of the volatile solvent, and in this case special varieties of percolator have been suggested. Such a volatile liquid percolator can be made with any ordinary percolator by fitting the lower orifice of the percolator with a cork, through which passes a glass tube, which in turn passes through another cork tightly fitted into the receiving bottle (Chapter XV. Then there must be an exit for the air from the receiving bottle, hence the receiving bottle must have two orifices, one provided with a glass tube connected by a rubber tube to the cork, tightly closing the top of the percolator; which cork, for convenience sake, is usually provided with a second orifice, through which passes a funnel for the admission of the solvent. In some work the use of the rubber tube connecting the receiving bottle with the top of the percolator is objected to on the grounds that the vapors of ether will attack the rubber of this tube, hence it is recommended that the outlet tube of the receiver be drawn to a fine, tapering point, to reduce loss of evaporation to the menstruum, a similar tapering tube being fitted in the cork closing the top of the percolator. The author's experience, however, has shown that the danger of destroying the rubber is scarcely worth considering, and not only by means of such rubber tubing is the loss by evaporation reduced to the minimum, but a steady flow of air from the receiving bottle to the top of the percolator ensues.

A modification of a volatile liquid percolator (Fig. 187), was used by the writer in a long series of experiments in percolation, from which he drew the conclusion that it would be highly profitable to use such a volatile liquid percolator for all cases of percolation.

BIBLIOGRAPHY

Extraction.—(Yield of extract) Lammer, A.Ph.A., 35, 1887, 35.

Maceration.—Webb, Dr. Circ., 42, 1898, 216.

Presses.—(History) Schelenz, Ch. Zt., 36, 1912, 397. (Hydraulic presses) Stabler, A.Ph.A., 12, 1864, 249; Rudd, Jl. A.Ph.A., 5, 1916, 170.

Percolation.—Snow, Ph. Rec., 7, 1887, 6; Kremers and Brandel, Ph. Rev., 24, 1906, 200, 311, and 340; 25, 1907, 57, 242, 273, 317 and 348; Keenan, Am. Dr., 56, 1910, 73; Couch, A.J.P., 91, 1919, 16 and 92, 1920, 770 and 853; (these four contributions give practically complete bibliographies, which include the following, of the subject as given in this chapter); Rumford, Ann. Phil., 9, 451; Real, Jl. ph. II, 2, 1816, 165; Boullay, Jl. de ph., 19, 1833, 281; and 21, 1835, 1; Robiquet, Jl. de ph., 21, 1835, 113; Duhamel, A.J.P., 10, 1838, 1; Duhamel and Procter, A.J.P., 11, 1839, 189.

Percolation.—(Principles) Goris, Bull. sci. pharmacol., through Pharm. J., 104, 1920, 225; Couch, see above; Hatcher, A.J.P., 93, 1921, 534; Prausnitz, Arch. d. Pharm., 268, 1930, 170; Husa and Magid, Jl. A.Ph.A., 23, 1934, 891, 980, 1097 and 1187; Wruble, A.J.P., 105, 1933, 244, 289 and 340. (Speed) Briedel and Barel, Jl. de ph. et ch. [8], 2, 1925, 49 and 476. (Menstrua) Scoville, Jl. A.Ph.A., 9, 1920, 864 and 868: 10, 1921, 844; 12, 1923, 104.

Percolators.—(Funnel) Squibb, A.Ph.A., 15, 1867, 392. (Cylindrical) Diehl, A.Ph.A., 27, 1879, 729; Oldberg, A.Ph.A., 32, 1884, 388. (Well tube) Squibb, A.Ph.A., 20, 1872, 182; and 26, 1878, 97. (Pressure) Rosewater, A.Ph.A., 30, 1882, 519. (Vacuum) Fairthorn, A.J.P., 54, 1882, 236. (Volatile liquid) Arny, A.Ph.A., 40, 1892, 169. (Continuous extraction) Soxhlet, Jl. Soc. Ch. Ind., 2, 1883, 57; Self and Corfield, Ph. Jl., 125, 1930, 98.

Percolating Appliances.—(Percolating shelf) Remington, A.J.P., 49, 1877, 589. (Percolator stopper) Zoeller, Am. Dr., 15, 1886, 103.

Diacolation.—Breddin, Ph. Zt., 76, 1931, 802.

PART II

INTRODUCTION

GALENIC PHARMACEUTIC PREPARATIONS

Having considered the processes used in pharmacy, we are now ready to study the application of these in the manufacture of pharmaceutic preparations.

For convenience in teaching we group pharmaceuticals into two classes—*galenic preparations* and *chemical preparations.* Those preparations in the manufacture of which no chemical action is involved are called galenic, after Galen, one of the ancient medical authorities, while chemical preparations are those in which a chemical change is produced during process of manufacture.

Already, in discussing Solution (p. 141), attention was called to the fallacy of the grouping into simple and chemical solution, from the strictly philosophic standpoint; yet, at the same time, the convenience of such grouping from the pharmaceutic point of view is readily admitted.

The same reasoning applies to a certain extent to the grouping of pharmaceuticals into galenic and chemical preparations, for many so-called "chemical preparations" can be made equally well by the retail pharmacist by purely galenic means. Thus, while the manufacture of syrup of hydriodic acid of the Pharmacopœia of 1890 involved a chemical reaction, the recipe of the present Pharmacopœia consists in merely mixing diluted hydriodic acid with water and sucrose (sugar). It is true that in making diluted hydriodic acid (U.S.P. IX) the same chemical reaction occurs that took place in making syrup of hydriodic acid (U.S.P. VII), but this does not apply as far as the present syrup is concerned, it being just as much a galenic as is syrup of citric acid.

As above mentioned, the classification of pharmaceuticals into galenic and chemical preparations, as far as this book is concerned, is merely a matter of convenience.

It would be manifestly absurd to discuss the manufacture of a preparation of which the most prominent feature is a chemical reaction, before considering the subject of chemistry as outlined in Part III; hence in all such preparations the discussion of their manufacture will be deferred until Part III is reached, and the only mention of them in this division will be the grouping of them under the heading Chemical Preparations in the list of officials found at the beginning of the discussion of each group of official pharmaceuticals.

The groups of official pharmaceuticals are given on the next page in a tabulated form:

LIQUID PREPARATIONS

I. Solutions of volatile substances:

Aqueous	*Waters.*
Alcoholic	*Spirits.*

II. Solutions of nonvolatile substances:

(*a*) Made by simple solution:

Aqueous	*Solutions.*
Aqueous (viscid)	*Mucilages.*
Aqueous (saccharine)	*Syrups.*
Mellifluous	*Honeys.*
Alcoholic	Some *tinctures*, as tincture of ferric chloride.
Alcoholic (saccharine)	*Elixirs.*
Glycerinic	*Glycerites.*
Ethereal	*Collodions.*
Oleaginous	*Oleates.*

(*b*) Made by maceration or percolation:

Aqueous	*Infusions* and *Decoctions.*
Alcoholic	*Tinctures* and *Fluidextracts.*
Vinous	*Wines* (U.S.P. IX).
Ethereal	*Oleoresins.*
Acetous	*Vinegars.*

III. Liquids containing undissolved matter:

(*a*) For internal use:

Aqueous, with neither oil nor resin	*Mixtures* and *magmas.*
Aqueous, with oil or resin	*Emulsions.*
Oily, for local application	*Sprays.*

(*b*) For external use:

Oleaginous	*Liniments* and *Petroxolins.*
Aqueous	*Lotions.*

SOLID PREPARATIONS

I. Made by maceration or percolation:

By evaporation	*Extracts* (*Abstracts,* U.S.P. 1880).
By precipitation	*Resins.*

II. Without maceration or percolation:

(*a*) For administration by mouth in unspecified portions:

Pulverized	*Powders, Effervescent Salts, Triturations,* and *Oil Sugars.*
Semisolid	*Masses.*
Semisolid (saccharine)	*Confections* (N.F. V).

In specified divided portions:

Globular doses	*Pills.*
Disc-like doses	*Tablets* and *Troches.*

(*b*) For administration by rectum, etc. .... *Suppositories.*

(*c*) For external administration:

Greasy masses—	
Applied as a plaster	*Cerates.*
Applied by inunction	*Ointments, Pastes,* and *Dressings.*
Nongreasy masses	*Jellies.*
Moist masses	*Cataplasms.*
Sticky masses	*Plasters.*
Spread on or absorbed by paper	*Papers* (N.F. V).

This grouping does not include such dental preparations as dentrifices, Dental Liniments, and Toothache Drops, nor does it include dosage forms such as ampuls which are really a class of "containers" of aqueous or oily solutions of medicinal substances of standardized strength, rather than "preparations."

CHAPTER XI

WATERS AND SPIRITS

WATERS

WATERS are *aqueous solutions of volatile substances,* not like spirits, which are alcoholic solutions of volatile substances; not like solutions, which are aqueous solutions of nonvolatile substances.

Again, the volatile substance may be solid, liquid, or gaseous. An example of an official water containing a volatile solid is found in camphor water; among those containing volatile liquids may be cited any of the official waters made from aromatic oils.

The following table gives a list of official waters grouped according to process of manufacture. Natural water, Aqua, N.F., is omitted from the table.

TABLE OF OFFICIAL WATERS

Process	*Galenic Preparations*	*Chemical Preparations*
Simple solution or dilution	*Ammonia water.* *Bitter almond water* (N.F.). *Camphor water.* *Chloroform water.* *Phenolated water* (N.F.). *Rose water.* *Wintergreen water* (N.F.).	
Gaseous solution		*Stronger ammonia water.* *Chlorine water* (U.S.P. 1890).
Distillation, cold solution or filtration through absorbent powder or paper	*Anise water.* *Cinnamon water.* *Fennel water.* *Peppermint water.* *Spearmint water.*	
Distillation	*Distilled water.* *Hamamelis water* (N.F.). *Orange flower water.* *Redistilled water* (N.F.). *Stronger rose water.*	
Sterilization	*Sterilized distilled water.*	

Simple Solution.—The process of preparing by *simple solution* or *dilution* consists in taking the constituent and adding to and agitating with a sufficient quantity of water. With those prepared by *gaseous solution* the gas is generated in an appropriate apparatus, and, after being washed, is passed into the cylinder containing the water, as explained on p. 147, usually the passage of the gas being continued until the solution is saturated with gas.

Some gases are much more soluble in water than others. Thus a 28 per cent aqueous solution of ammonia gas can be prepared, while a saturated chlorine water contains only 0.4 of 1 per cent of that gas.

Hot-water Process.—A method of manufacture of aromatic waters not given official sanction is by *solution in hot water.* This consists in agitating volatile substances with hot water, a process recommended by several pharmaceutic writers. The process, however, is not official, and the Pharmacopœia has been wise in omitting it, for the reason that the use of hot water occasions considerable loss through the evaporation of the volatile substance. Again, it may be cited that the use of hot water does not produce more saturated products; experiments have shown that when the waters so prepared are brought to the normal temperature and filtered until perfectly clear, their strength is no greater than those made by other processes. As a possible advantage of the use of hot water it has been said that the process afforded more rapid solution than any other process. But, admitting this to be true, it is more than counterbalanced by the inconvenience of agitating a hot bottle with the possible blowing out of the cork, to say nothing of the danger of fracturing the glass container.

Filtration through Absorbents.—This process also referred to as *solution by intervention* when the absorbent is an insoluble powder, is employed to obtain a saturated solution of a volatile oil. Volatile oils are very sparingly soluble in water, and, in the attempt to facilitate solution, the oil is separated into a finely divided form by trituration with an absorbent powder, or paper pulp and water is then gradually added. The absorbents employed for this purpose in earlier Pharmacopœias were magnesium carbonate and precipitated calcium phosphate. Waters prepared by the intervention of either one of these powders are unsatisfactory. Magnesium carbonate dissolves in water in appreciable amounts, and an aromatic water prepared in this way will very frequently precipitate chemicals one desires to dissolve therein. Calcium phosphate was chosen by the Pharmacopœia of 1890 by reason of its supposed insolubility; but investigation showed that while calcium phosphate is not so soluble as magnesium carbonate, the minute traces which do dissolve cause more mischief than does the magnesium carbonate; the calcium phosphate acting as pabulum for the spores of microscopic organisms which may lodge in the water, forming flocculent, slimy masses, due to the development of these organisms. For this reason, purified talc was chosen as the absorbent powder in the U.S.P. X and in the present Pharmacopœia a choice of talc, purified silicious earth or pulped filter paper is permitted. Other absorbents used and recommended by practising pharmacists of an earlier generation were shredded absorbent cotton (used in U.S.P. method prior to 1890) and pulped filter paper. The oil was dropped on the shredded cotton or paper pulp and the latter were packed into a funnel or percolator. As the water percolated through the cotton or paper it became fairly well saturated with the oil. This method does not furnish as good a product as filtration through an absorbent powder, nor is it superior to the addition of a volatile oil to cold water, shaking at intervals during twenty-four hours and filtering. It is however a speedier method than the latter.

Distillation.—This process was the first way in which aromatic waters were prepared, and yields the finest product. The process of distillation has been fully described in Chapter V, and here need only be mentioned the modifications of the process adapted for the product under consideration.

The substances from which the volatile principles are to be obtained are suspended in a boiler or a still, and are never permitted to lie on the surface of the boiler next to the flame, for in such a case the heat produces a decomposition, and the product will be ruined through presence of empyreumatic odors. Into the still a requisite quantity of water is poured and is heated on a slow fire, and, as the vapors rise from the boiler, they carry with them the aromatic principles found in the plant. If enough of the substance is used, a considerable excess of the oil may be found floating on the surface of the distillate. In fact, most distilled waters are made on a large scale as the side product in the distillation of volatile oils (see p. 840).

Distilled rose water and orange flower water of commerce are termed simple distilled, double distilled, triple distilled, or quadruple distilled, according to strength.

A double distilled water is prepared by mixing 1 part of flowers with say, 2½ parts of water, and collecting 2 parts of distillate; triple distilled is made by distilling off 1 part of distillate from 1½ parts of flowers; while quadruple distilled is made by securing 1 part of distillate from 1 part of flowers; hence the triple distilled is stronger than the quadruple distilled. In some cases, in preparing quadruple distilled water, another 1 part of flowers is mixed with sufficient double distilled water, and 2 parts distillate obtained. This process of redistilling is called *cohobation*.

In most of the modern perfume factories the distillation over a naked fire has been supplanted by distilling in steam. In this case steam is passed into an appropriate iron vessel containing the aromatic substance and in passing through it carries the odor along with it.

The preservation of distilled waters is not an easy matter by reason of the fact that such solutions afford a nidus for the growth of microscopic organisms. It has been observed that the growth of these organisms is furthered by the corking of the containers, and in the warehouses of the large aromatic water distillers the waters are kept in carboys, which are closed with a pledget of cotton instead of being corked.

The term "aromatic waters" has reference to that class of waters which are made from odorous principles, and are used chiefly to supply aromatic odors and flavorings. This includes all the official waters except the ammonia waters, chloroform water, phenolated water, hamamelis water, and chlorine water (U.S.P. 1890).

Special Notes on Official Waters.—Before discussing the several official waters, a few words explanatory of the order of presentation of these and other galenic preparations may not come amiss. Having already given the general methods of manufacture and a table of the official representatives of this class of preparations, at this place reference need only be made to the individual peculiarities of each of the several preparations, which will be presented in alphabetic order, except in cases where other arrangements are advisable. The official recipe for many of the same class of galenics is identical, save the constituents, and, therefore, in order to avoid "vain repetition," the pharmacopœial recipes will be given at length only in one case, and under the other preparations made by the identical process will be the reference to the typical recipe, with a note as to the deviations in making the preparation under consideration. To be specific, in the class of aromatic waters the five official waters—anise, cinnamon, fennel, peppermint, and spearmint—are made by exactly similar processes; by distillation, solution in cold water or by filtration through the absorbent powder or pulp; the only difference being the employment of the specific oil needed to make the particular flavor desired. Hence in giving the condensed recipe reference will be made in each case to the "General Formula" under Aquæ Aromaticæ. If no recipe is prescribed by the Pharmacopœia, mention of the fact will be given.

Again, as already mentioned, Part II is not the proper place to discuss the chemistry of manufacture of such official preparations as are more chemical than pharmaceutic; hence in such cases discussion of manufacture will be left for Part III, and the fact so noted.

Lastly, these arrangements will obtain as far as possible in all the different classes of preparations discussed in Part II. In the case of tinctures and fluidextracts, where scores of each class of preparations are made by a process identical, save in choice of menstruum and fineness of powder, an outline of the U.S.P. recipe will be given in the case of the first of a general class of products and in discussing others in the same class, reference will be made to the first formula with such changes as may be necessary in any particular case.

AQUÆ AROMATICÆ—Aromatic Waters

Under this heading, the Pharmacopœia (p. 68) gives a general formula suggesting distillation, cold solution or filtration through absorbent powder. In the 2 cases last mentioned it is directed that 2 cc. of the oil or other volatile substance or 2 Gm. if the substance is a solid, be used in making 1000 cc. of the aromatic water. It also directs the use of 15 Gm. of purified talc or a sufficient quantity of purified siliceous earth or pulped filter paper in making 1000 cc. of the water.

Remarks.—The above statement gives pharmacopœial sanction to the manufacture of aromatic waters by the several processes there enumerated.

AQUA AMMONIÆ and AQUA AMMONIÆ FORTIOR

Both are solutions of the chemical, ammonia, and will be described on p. 502.

AQUA ANISI—Anise Water

(Aq. Anisi)

Anise Water is a saturated solution of oil of anise in distilled water, prepared by one of the processes described under *Aquæ Aromaticæ.*

Remarks.—It is frequently stated that the percentage of oil in anise water is 0.2 of 1 per cent since the General Formula calls for 2 cc. of oil to 1000 cc. of water. This conclusion however, is incorrect, inasmuch as scarcely more than half of the oil is dissolved by the water, the rest remaining on the filter.

Dose.—15 mils (4 fluidrachms).

AQUA AURANTII FLORUM—Orange Flower Water

(Aq. Aurant. Flor.)

Orange Flower Water is a saturated solution of the odoriferous principles of the flowers of *Citrus Aurantium* Linné (Fam. *Rutaceæ*), prepared by distilling the fresh flowers with water and separating the excess volatile oil from the clear, aqueous portion of the distillate. Its odor is best preserved by allowing a limited access of fresh air to the container.

Source.—The commercial article.

Description.—Colorless and only faintly opalescent, with pleasant orange flower odor and taste.

Impurities.—Metals. Test with hydrogen sulfide or sodium sulfide. For details see U.S.P., p. 64.

Manufacture.—No recipe is given by the Pharmacopœia, but this water is made by cohobation, as already described on p. 196, the commercial article being "triple distilled."

Remarks.—The metallic impurity test given above is intended to prevent use of a water that has been kept too long in the copper containers (usually tin lined) in which the commercial article is usually shipped.

Medical Properties.—Flavor and mild sedative.

Orange flower water, like other distilled waters, develops a "stringiness" due to micro-organisms. Guyot finds that the chief cause of this flocculent deposit is *Hydrocrocis hydrolatorum*. Sometimes this growth assumes a green color due to infection with the nontoxic bacterium, *Bacillus chloroaphis*.

AQUA CAMPHORÆ—Camphor Water

(Aq. Camph.)

Camphor Water is a saturated solution of camphor in distilled water, prepared by solution of the camphor as described under *Aquæ Aromaticæ*.

Remarks.—Camphor water is one of the few official waters in which the base is not a volatile oil. In making it the camphor is dissolved in water by cold solution; not being previously dissolved in alcohol, as directed in former Pharmacopœias.

Dose.—10 cc. (2½ fluidrachms).

AQUA CHLOROFORMI—Chloroform Water

(Aq. Chlorof.)

Condensed Recipe.—Chloroform and distilled water, of each a sufficient quantity, are mixed together in a dark amber-colored bottle; enough chloroform being used to insure a slight excess after a saturated aqueous solution is obtained. For details, see U.S.P., p. 65.

Storage.—Preserve in well-closed containers and protected from light.

Remarks.—The above recipe is a modification of the process of simple solution, the finished product being kept over a layer of chloroform. This is done in order that the finished product remain a saturated solution, experience proving that a filtered chloroform water soon loses all its volatile active principle, leaving nothing but ordinary water. The saturated solution contains about ½ of 1 per cent of chloroform. When chloroform water is to be dispensed the required quantity is decanted. Care should be taken *not* to shake the bottle before dispensing. It should be kept in well-closed containers and protected from light.

Dose.—15 cc. (4 fluidrachms).

AQUA CINNAMOMI—Cinnamon Water

(Aq. Cinnam.)

Cinnamon Water is a saturated solution of oil of cinnamon in distilled water, prepared by one of the processes described under *Aquæ Aromaticæ*.

Remarks.—Cinnamon water belongs to the same class as anise water, made by the same method, and the remarks applied to the strength of anise water are equally forcible in the case of the water under consideration. It must be borne in mind that the oil of cinnamon from which the water is made is very irritating, and often in the dilution found in cinnamon water the taste is decidedly biting. For this reason the Pharmacopœia directs, when making chalk mixture, that the cinnamon water be used diluted with a quantity of water, as explained on p. 279.

Dose.—15 cc. (4 fluidrachms).

AQUA DESTILLATA, AQUA DESTILLATA STERILISATA, and AQUA REDESTILLATA

These officials being chemicals rather than pharmaceuticals, will be discussed in Part III.

AQUA FŒNICULI—Fennel Water

(Aq. Fœnic.)

Fennel Water is a saturated solution of oil of fennel in distilled water, prepared by one of the processes described under *Aquæ Aromaticæ*.

Dose.—15 cc. (4 fluidrachms).

AQUA MENTHÆ PIPERITÆ—Peppermint Water

(Aq. Menth. Pip.)

Peppermint Water is a saturated solution of oil of peppermint in distilled water, prepared by one of the processes described under *Aquæ Aromaticæ*.

Dose.—15 cc. (4 fluidrachms).

AQUA MENTHÆ VIRIDIS—Spearmint Water

(Aq. Menth. Vir.)

Spearmint Water is a saturated solution of oil of spearmint in distilled water, prepared by one of the processes described under *Aquæ Aromaticæ*.

Dose.—15 cc. (4 fluidrachms).

AQUA ROSÆ—Rose Water

(Aq. Ros.)

Recipe.—Dilute stronger rose water with equal quantity of distilled water immediately before use.

AQUA ROSÆ FORTIOR—Stronger Rose Water

(Aq. Ros. Fort.)

A saturated solution of odoriferous principles of the flowers of *Rosa centifolia* Linné (Fam. *Rosaceæ*) prepared by distilling the fresh flowers with water and separating the excess volatile oil from the clear aqueous portion of the distillate. Its odor is best preserved by allowing a limited access of fresh air to the container.

Source.—The commercial article.

Description.—Clear and colorless liquid, smelling like roses.

Impurities.—Metals. Test with hydrogen sulfide or sodium sulfide. For details, see U.S.P., p. 68.

Manufacture.—No recipe given by the Pharmacopœia, but it is a triple distilled water.

Remarks.—The two varieties of rose water may be discussed together. Stronger Rose Water is a triple distilled water even as orange flower water is. Rose Water, without further qualifications, means the distilled rose water diluted with an equal volume of distilled water.

Aqua Amygdalæ Amaræ (U.S.P. IX, N.F. VI), or *Bitter Almond Water*, is made by dissolving 1 cc. of oil of bitter almond in enough recently boiled distilled water to make 1000 cc. The strength of this water (1/10 of 1 per cent of oil) *does* not coincide with the international standard (p. 28) which directs a content of 1/10 of 1 per cent of hydrocyanic acid.

Aqua Chlori (U.S.P. 1890).—*Chlorine Water.*—The process of manufacture of this water will be found on p. 421, as this is not the proper time to consider the chemical action. Chlorine water is a preparation which should be made freshly each time it is dispensed. The National Formulary V provides a simple extemporaneous process for preparing a similar preparation, *liquor chlori compositus.*

Aqua Gaultheriæ (N.F. VI).—*Wintergreen Water* is made by dissolving 5 cc. of oil of gaultheria (U.S.P.) in sufficient distilled water to make 1000 cc.

Aqua Hamamelidis (U.S.P. IX; N.F. VI) or *Hamamelis Water,* is made by distilling the twigs and leaves of the shrub, *Hamamelis virginiana.* It is commonly called *distilled extract of witch hazel* and has attained widespread popularity through the persistent advertising of one of its proprietary forms. Its therapeutic value is doubtful, many authorities claiming that its sole virtue resides in the alcohol it contains. Of particular importance to the retailer is the Formulary requirement that this product contain 14 per cent *grain* alcohol (ethyl alcohol of the Pharmacopœia), and that no formaldehyde, methyl alcohol, acetone or iso-propyl alcohol be present. It is to be kept in well-closed containers, in a cool place.

Aqua Phenolata N. F. is made by dissolving 22 cc. of liquefied phenol in 978 cc. of distilled water.

Medical Properties of Waters.—The medical properties of most pharmaceutic preparations are those of the drugs from which they are obtained, and therapeutic consideration will be found in the proper place under the drug which is the leading ingredient.

In some few cases, however, the preparation consists of a blending of ingredients giving different action than the constituent drugs; or possibly may be a commercial, ready-made article, the constituents of which are not official. In such cases, illustrated in this chapter in orange flower water, the medical properties will be discussed at the time the preparation is considered.

Waters as a class are usually such diluted preparations that they are scarcely used as medicines, but are generally employed as vehicles. As notable exceptions, however, must be cited such waters as the ammonia waters and chlorine water; these, being rather powerful preparations and having special uses, will be considered in their place among the chemicals.

DOSES OF OFFICIAL WATERS

1 cc. (15 minims)	Ammonia water.
10 cc. (2½ fluidrachms)	Camphor water.
15 cc. (4 fluidrachms)	Anise water, chloroform water, cinnamon water, fennel water, peppermint water, spearmint water.
No dose given	Orange flower water, the rose waters, bitter almond water, hamamelis water, phenolated water.

Stronger ammonia water should never be dispensed for administration by a patient, it being recognized by the Pharmacopœia merely as a standard form of ammonia which can be diluted to a 10 per cent strength when required.

SPIRITS

A spirit is *an alcoholic solution of a volatile substance,* and, therefore, spirits differ from waters only in the solvent employed. For this reason a number of spirits are made from substances which are also used in the manufacture of waters. Practically all the volatile oils represented in the list of aromatic waters are found in alcoholic solution among the spirits. The number of spirits, however, is larger than that of the waters, due to the superior solubility of oils in alcohol. Moreover, the amount of oils found in spirits is much greater than that found in waters, most of the spirits containing from 5 to 10 per cent or even 20 per cent of the oil.

TABLE OF OFFICIAL SPIRITS

Manufacture	*Galenic Preparations*	*Chemical Preparation*
Simple solution or dilution.	Spirit of ammonia, aromatic.	Spirit of ethyl nitrite. Spirit of glyceryl trinitrate.
	Spirit of ammonia, anisated (N.F.)	
	Spirit of anise.	
	Spirit of bitter almond (N.F.)	
	Spirit of camphor.	
	Spirit of cardamom, compound (N.F.)	
	Spirit of chloroform.	
	Spirit of cinnamon.	
	Spirit of ether (N.F.)	
	Spirit of ether, compound (N.F.)	
	Spirit of formic acid (N.F.)	
	Spirit of lavender.	
	Spirit of myrcia, compound (N.F.)	
	Spirit of orange, compound.	
	Spirit, perfumed (N.F.)	
	Spirit of vanillin, compound (N.F.)	
Gaseous solution	Spirit of ammonia (U.S.P. VIII).	
Solution with maceration	Spirit of peppermint.	
	Spirit of spearmint.	
Distillation	Whisky.	
	Brandy.	

As is seen in the above chart, the official spirits are made in three different ways:

Simple Solution or Dilution.—This process is simply adding and dissolving the medicated substance in alcohol. (In this group we find fifteen of the twenty-one official spirits.) A general formula for *spirits of volatile oils* is given in the National Formulary.

Solution by Maceration.—Two official spirits are made in this way—peppermint and spearmint. In each case the flavoring constituent is a volatile oil, but in deference to the wishes of the public who desire a spirit colored like the drug from which it is made, the Pharmacopœia directs that, after the oil is added to the alcohol, it is to be macerated with some of the drug until the color of the latter has been absorbed by the alcohol.

Distillation.—Two spirits of the Pharmacopœia—*whisky* and *brandy*—are prepared by distillation.

Two official spirits may be considered as made by *chemical action*—spirit of glyceryl trinitrate and spirit of nitrous ether. In neither case, however, does the Pharmacopœia give directions for the preparation of the chemical, glyceryl trinitrate or ethyl nitrite. It is considered too dangerous for the ordinary drug store to manufacture nitroglycerin or the spirit of this compound, while in the case of the spirit of nitrous ether, the spirit is really made by dissolving the finished ethyl nitrite in alcohol, and the process may, therefore, be considered as a case of simple solution or dilution. The highly volatile nature of ethyl nitrite makes it extremely difficult to manufacture a satisfactory preparation under the ordinary conditions of a retail pharmacy. For this reason both of these preparations are found in the chart given above under the head of simple solution or dilution.

SPECIAL NOTES ON OFFICIAL SPIRITS

SPIRITUS ÆTHYLIS NITRITIS—Spirit of Ethyl Nitrite

A full explanation of this important preparation, commonly called *sweet spirit of nitre*, will be found on p. 662.

SPIRITUS AMMONIÆ AROMATICUS—Aromatic Spirit of Ammonia

This important pharmaceutical can best be considered under the Ammonium compounds (p. 506).

SPIRITUS ANISI—Spirit of Anise

(Sp. Anisi)

Spirit of Anise contains, in each 100 cc., not less than 9 cc. and not more than 11 cc. of oil of anise.

Recipe.—Dissolve 100 cc. oil of anise in enough alcohol to make 1000 cc.

Assay.—See U.S.P., p. 352.

Remarks.—This is a 10 per cent preparation made by simple solution. Bear in mind that the alcohol of the present Pharmacopœia is equivalent to the deodorized alcohol (Cologne Spirits) of the Pharmacopœia of 1890, and is devoid of the unpleasant odor which alcohol that does not come up to U.S.P. specifications leaves on evaporation. In the preparation of essences made from fine oils the U.S.P. alcohol must be used. Alcohol from other sources or recovered from some manufacturing process is not satisfactory.

Dose.—1 cc. (15 minims).

SPIRITUS AURANTII COMPOSITUS—Compound Spirit of Orange

(Sp. Aurant. Co.)

Compound Spirit of Orange contains, in each 100 cc., not less than 25 cc. and not more than 30 cc. of the mixed oils.

Storage.—Preserve in well-closed containers and protected from light.

Condensed Recipe.

Ingredients.—Oil of orange, 200 cc.; oil of lemon, 50 cc.; oil of coriander, 20 cc.; oil of anise, 5 cc.; alcohol, enough to make 1 liter.

Manipulation.—Mix the oils with the alcohol. For details, see U.S.P., p. 352.

Assay.—See U.S.P., p. 353.

Remarks.—This preparation, used as the flavor in *aromatic elixir* (p. 226), must be made of the best oils and alcohol if it is to be satisfactory. The official provision as to storing in well-closed containers and protected from light, is to prevent the oils from growing terebinthinate.

SPIRITUS CAMPHORÆ—Spirit of Camphor

(Sp. Camph.)

Spirit of Camphor is an alcoholic solution containing, in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of camphor, at 25° C.

Condensed Recipe.—Dissolve 100 Gm. camphor in 800 cc. of alcohol and then add enough alcohol to make 1 liter, filtering if necessary.

Impurity.—Added water. See U.S.P., p. 353.

Assay.—See U.S.P., p. 353.

Remarks.—Note that the recipe of the Pharmacopœia does not direct the addition of water, and provides a test for the presence of water as well as gravimetric assay for the spirit. The addition of water is therefore considered by drug control officials as an adulteration.

Dose.—1 cc. (15 minims).

SPIRITUS CHLOROFORMI—Spirit of Chloroform

(Sp. Chlorof.)

Spirit of Chloroform contains, in each 100 cc., not less than 8.5 Gm. and not more than 9.25 Gm. of $CHCl_3$ at 25° C.

Storage.—Preserve in well-closed containers and protected from light.

Recipe.—Made by dissolving 60 cc. chloroform in enough alcohol to make 1 liter.

Assay.—See U.S.P., p. 354.

Dose.—2 cc. (30 minims).

SPIRITUS CINNAMOMI—Spirit of Cinnamon

(Sp. Cinnam.)

Spirit of Cinnamon contains, in each 100 cc., not less than 9 cc. and not more than 11 cc. of oil of cinnamon.

Recipe.—Made by dissolving 100 cc. oil of cinnamon in enough alcohol to make 1 liter.

Assay.—See U.S.P., p. 354.

Dose.—1 cc. (15 minims).

SPIRITUS FRUMENTI—Whisky

This product will be discussed among the alcoholic beverages (p. 659).

SPIRITUS GLYCERYLIS TRINITRATIS—Spirit of Glyceryl Trinitrate

This very important official, Spirit of Nitroglycerin, is fully described on p. 680.

SPIRITUS LAVANDULÆ—Spirit of Lavender

(Sp. Lavand.)

Spirit of Lavender contains, in each 100 cc., not less than 4 cc. and not more than 6 cc. of oil of lavender.

Recipe.—Oil of lavender, 50 cc. Alcohol, enough to make 1 liter.

Assay.—See U.S.P., p. 357.

Dose.—2 cc. (30 minims).

SPIRITUS MENTHÆ PIPERITÆ—Spirit of Peppermint

(Sp. Menth. Pip.—Essence of Peppermint)

Spirit of Peppermint contains, in each 100 cc., not less than 9 cc. and not more than 11 cc. of oil of peppermint.

Storage.—Preserve in well-closed containers and protected from light.

Condensed Recipe.

Ingredients.—Oil of peppermint, 100 cc.; peppermint, 10 Gm.; alcohol enough to make 1 liter.

Manipulation.—Macerate the peppermint leaves with water during one hour and then strongly express them. Add the peppermint leaves to 900 cc. of alcohol and macerate six hours. After filtration add the oil and run through the filter enough alcohol to make 1 liter. For details, see U.S.P., p. 358.

Assay.—See U.S.P., p. 358.

Remarks.—This is a 10 per cent preparation of the oil of peppermint made with alcohol, and macerated with sufficient peppermint leaves to give it a green color. It is not to be confused with the Flavoring *Extract* of Peppermint which contains considerably less oil of peppermint.

Dose.—1 cc. (15 minims).

SPIRITUS MENTHÆ VIRIDIS—Spirit of Spearmint

(Sp. Menth. Vir.)

Spirit of Spearmint contains, in each 100 cc., not less than 9 cc. and not more than 11 cc. of oil of spearmint.

Storage.—Preserve in well-closed containers and protected from light.

Recipe.—Oil of spearmint, 100 cc.; spearmint (bruised), 10 Gm.; alcohol, to make 1000 cc. Make exactly as in recipe for spirit of peppermint.

Assay.—See U.S.P., p. 359.

Dose.—1 cc. (15 minims).

SPIRITUS VINI VITIS—Brandy

This alcoholic beverage is discussed on page 659.

SPIRITUS OLEORUM VOLATILIUM—Spirits of Volatile Oils

Under this heading the National Formulary gives a general formula for the preparation of any spirit of a volatile oil for which no other formula is provided. It calls for 65 cc. of the volatile oil and enough alcohol to make 1 liter.

Spiritus Ætheris (U.S.P. IX; N.F. VI) is made by dissolving 325 cc. of ether in alcohol enough to make 1 liter. It is sold in German sections under the name of *Hoffmann's Drops.* It should be kept in well-closed containers, protected from light.

Spiritus Ætheris Compositus (U.S.P. VIII; N.F. VI) is prepared by mixing 325 cc. of ether, 650 cc. of alcohol and 25 cc. of ethereal oil. It is usually called *Hoffmann's Anodyne* and because of the presence of the expensive ethereal oil (p. 664) is liable to be adulterated. It should therefore be prepared by the pharmacist from an ethereal oil of known reliability. It should be kept in well-closed containers, protected from light.

Spiritus Ammoniæ (U.S.P. VIII) is made by gaseous solution and like ammonia water contains 10 per cent of ammonia gas (p. 503).

Spiritus Amygdalæ Amaræ (U.S.P. IX; N.F. VI) or *Spirit of Bitter Almond,* is made by dissolving 10 cc. of oil of bitter almond in 800 cc. of alcohol and then adding enough water to make 1000 cc. It should not be sold as "essence of bitter almond" since it is made from an oil containing hydrocyanic acid (p. 794); hence it is not safe to use indiscriminately (U. S. Dept. Agr.). Essences or flavoring extracts should, of course, be harmless alcoholic preparations of aromatic principles and in making a flavoring essence of almond, an oil that has been freed from hydrocyanic acid should be employed. Among the harmless "essences" might be cited spirit of peppermint, spirit of spearmint and also spirit of lemon, U.S.P., 1890. Essence of ginger and essence of vanilla are respectively tincture of ginger and tincture of vanilla. The spirit of bitter almond, it might be worth noting, contains about 20 per cent of water.

Spiritus Juniperi (U.S.P. IX) and **Spiritus Juniperi Compositus** (U.S.P. IX) were dropped from the Pharmacopœia since both preparations might be considered as disguised "tipples." The compound spirit of juniper was frankly intended as a synthetic gin; the genuine gin being made by distilling fermented rye and malt, macerating the distillate with juniper berries and then redistilling the mixture.

Spiritus Limonis (U.S.P., 1890) is now replaced by the official *tincture of lemon peel* (p. 249). The spirit (*essence of lemon*) is prepared by dissolving 50 cc. of oil of lemon in 950 cc. of alcohol and then macerating in the mixture 50 Gm. of grated lemon peel, which gives the product a yellow color. The oil used should be free from terebinthinate odor and the alcohol should be strictly pharmacopœial.

Spiritus Phosphori (U.S.P., 1890) is a 1 per cent solution of phosphorus, made with absolute alcohol by the process of upright condensation. (See p. 121.) This process was employed to save undue evaporation of alcohol, it being necessary to digest the phosphorus in boiling alcohol for several hours in order to dissolve it. When this process is carried on in an ordinary flask, a large amount of alcohol would be lost by evaporation, but if the upright condenser is inserted in the neck of the flask, the vapor of alcohol passing through the cold condensing tube is converted into liquid, and drops back into the flask from which it has just emerged. Spirit of phosphorus was official because an ingredient of the *elixir of phosphorus* of the Pharmacopœia of 1890.

THE SPIRITS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 mils).	Remarks.
Spiritus acidi formici.	Spiritus formicarum; spirit of ants.	Formic acid, 40 cc.; distilled water, alcohol.	*Dose.*—4 cc (1 fluidrachm).
Spiritus ætheris.	Hoffmann's drops.	Ether, 325 cc.; alcohol.	*Dose.*—4 cc. (1 fluidrachm).
Spiritus ætheris compositus	Hoffmann's anodyne.	Ether, 325 cc.; ethereal oil, 25 cc. alcohol.	*Dose.*—4 cc. (1 fluidrachm).
Spiritus ammoniæ anisatus.	Liquor ammoniæ anisatus.	Anethol, 30 cc.; ammonia water; alcohol.	*Dose.*—1 cc. (15 minims).
Spiritus amygdalæ amaræ.	Spirit of almond.	Oil of bitter almond, 10 cc.; alcohol; distilled water.	*Dose.*—0.5 cc. (8 minims).
Spiritus cardamomi compositus.	Compound spirit of cardamom.	Oils of cardamom, sweet orange, cinnamon, clove and caraway; anethol, alcohol	Flavoring used in making elixirs.
Spiritus myrciæ compositus.	Compound spirit of myrcia.	Oils of myrcia, sweet orange and pimenta; alcohol; water.	A well-perfumed form of *bay rum*.
Spiritus odoratus.	Perfumed Spirit, Cologne water.	Oils of bergamot, lemon, rosemary, lavender and orange flowers; ethyl acetate; water; alcohol.	An agreeable form of *cologne water*.
Spiritus vanillini compositus.	Compound spirit of vanillin.	Vanillin; oils of orange, cardamom and cinnamon, alcohol	Used in flavoring elixirs.

DOSES OF SPIRITS

0.06 cc. (1 minim)	Spirit of glyceryl trinitrate.
0.5 cc. (8 minims)	Spirit of bitter almond.
1 cc. (15 minims)	Spirits of anise, camphor, cinnamon, peppermint, spearmint, and ammonia anisated.
2 cc. (30 minims)	Spirits of ethyl nitrite, ammonia aromatic, chloroform, and lavender.
4 cc. (1 fluidrachm)	Spirit of formic acid; ether; ether compound.

BIBLIOGRAPHY

Waters.—(Manufacture by hot process) Ebert, A.Ph.A., 19, 1871, 143. (Absorbent powder) Sheppard, A.Ph.A., 19, 1871, 442. (Shredded paper) Igel, Am. Dr., 16, 1887, 217. (Kieselguhr) La Wall, A.Ph.A., 57, 1909, 252. (Cold solution) Arny, A.Ph.A., 46, 1898, 234. (Distillation) Piesse, Art of Perfumery, p. 203.

Distilled Extract of Witch Hazel.—Dickinson, Pharm. Era. 35, 1906, 62; Hilton, Jl. A.Ph.A., 19, 1930, 232.

Distilled Waters.—(Fungoid growths in) Tait, Ph. Jl., 87, 1911, 886; Guyot, J. ph. ch., 13, 1916, 37 and 15, 1917, 12.

Spirits.—(Manufacture) Simm, Ph. Jl., 107, 1921, 519; Terry, A.J.P., 100, 1928, 625. (Bay rum) Gordon, Dr. Circ., 55, 1911, 183; Anon., *ibid.*, 63, 1919, 190. (Camphor) Schoorl, Ph. Weekbl., 66, 1929, 977 and 1001. (Hoffmann's anodyne) Procter, A.J.P., 24, 1852, 213.

CHAPTER XII

SOLUTIONS, MUCILAGES, SYRUPS, AND HONEYS

SOLUTIONS

Solutions constitute that class of pharmaceuticals defined as "*aqueous solutions of nonvolatile bodies.*" This definition is redundant, inasmuch as we say that a "solution" (the class of pharmaceuticals) is a "solution" (that is, a product of the physical phenomenon called solution, which has been discussed on p. 142.) In other words, the student at the outset should get a clear idea of the three meanings of the word "solution." First, the physical phenomenon of molecular subdivision resulting in a homogeneous fluid; second, the physical group of solutions, those homogeneous fluids produced by molecular subdivision, and including such pharmaceuticals as waters, spirits, glycerites, tinctures, etc.; and, third, the narrow pharmaceutic "solution," which is limited only to that class of physical solutions which have water as the solvent and a nonvolatile body as dissolved substance.

A pharmacopœial solution is an aqueous preparation, free from sugar (exception, Solution of Magnesium Citrate), made by the ordinary process of solution. Some writers divide this class into simple and chemical solutions, while others oppose such a distinction, claiming there is no real difference in the liquefaction occurring in, say, solution of arsenous acid and in solution of ferric acetate. The latter class of writers claim that the chemical combination occurring in the formation of a so-called "chemical solution" has nothing to do with the act of solution, the chemical reaction first occurring, then being followed by the solution of the newly formed substance or of the ions of which it is composed. (See p. 142.) There is much truth in the argument that the arsenous acid in the first solution cited above is produced by chemical reaction, as much as is the ferric acetate in the other preparation; that the fact whether the substance is dissolved at the moment of formation or after some time has elapsed makes little difference.

In this book we will divide solutions into galenic preparations (simple solutions) and into chemical preparations (chemical solutions), for the same reason that we group all pharmaceuticals into the two classes; that in Part II we will discuss only these preparations made without chemical action, leaving those in which a chemical action occurs for consideration in Part III.

The manufacture of solutions is simple or complex, according as the preparation is a galenic or a chemical. Galenic solutions are prepared by simply dissolving the substance in an appropriate quantity of water in either a flask or a bottle, by agitation, or by first reducing the substance to a fine powder by trituration in a mortar, and gradually adding water to the substance in the mortar.

The preparation of the so-called "simple solutions" is an easy matter —so easy that the average druggist is grossly careless with them. They should be elegant preparations; hence the careful pharmacist is generous with his filter paper, having all his solutions (save possibly lead water) as clear as crystal. This applies to all solutions, and especially to extemporaneous prescriptions. Have all preparations, intended to be clear, fairly sparkling, for the only method possessed by the public of judging the skill of the pharmacist is the appearance of his preparations and the neatness of his packages.

The chemical solution, on the other hand, usually requires a high degree of skill in its manufacture, and the description of this class had best be left until we consider the substance from the chemical aspect in Part III. The following table gives a list of officials arranged as galenic or chemical:

TABLE OF OFFICIAL SOLUTIONS

Manufacture	*Galenic Preparations*	*Chemical Preparations*
These galenics are made by simple solution.	Antiseptic solution (N.F. VI). Solution of aluminum chloride (N.F. VI). Solution of amaranth (N.F. VI). Solution of arsenic and mercuric iodides (N.F. VI). Solution of arsenous acid. Solution of boric acid (N.F. VI). Solution of calcium hydroxide. Solution of carmine (N.F. VI). Solution of cochineal (N.F. VI). Solution of ephedrine sulfate (N.F. VI). Solution of epinephrine hydrochloride. Solution of formaldehyde. Solution of histamine phosphate. Solution of hydrogen peroxide. Solution of iodine, compound. Solution of lead subacetate, diluted (N.F. VI). Solution of methyl-rosaniline (N.F. VI). Solution of nux vomica alkaloids (N.F. VI). Solution of peptonized iron (N.F. VI). Solution of peptonized iron and manganese (N.F. VI). Solution of potassium hydroxide (N.F. VI). Solution of potassium iodide (N.F. VI). Solution of procaine hydrochloride (N.F. VI). Solution of soda and mint (N.F. VI). Solution of sodium arsenate (N.F. VI). Solution of sodium borate, compound (N.F. VI). Solution of sodium phosphate (N.F. VI).	Alkaline aromatic solution (N.F. VI). Solution of aluminum acetate (N.F. VI). Solution of aluminum subacetate (N.F. VI). Solution of ammonium acetate. Solution of cresol, saponated. Solution of ferric chloride. Solution of ferric subsulfate (N.F. VI). Solution of ferric sulfate. Solution of iodine, phenolated (N.F. VI). Solution of iron and ammonium acetate (N.F. VI). Solution of lead subacetate (N.F. VI). Solution of magnesium citrate. Solution of sulfurated lime (N.F. VI). Solution of potassium arsenite. Solution of potassium citrate (N.F. VI). Solution of sodium citrate (N.F. VI). Solution of sodium hypochlorite. Solution of sodium hypochlorite, diluted.
These galenics are made by simple solution and sterilization.	Isotonic solution of dextrose and sodium chloride (N.F. VI). Physiological solution of sodium chloride.	
This galenic is made by extraction and solution.	Solution of liver.	
These galenics are made by extraction, solution, and sterilization.	Solution of liver, purified. Solution of parathyroid. Solution of posterior pituitary.	
This galenic is made by solution and irradiation.	Solution of irradiated ergosterol.	
This galenic is made by maceration.	Solution of coal tar (N.F. VI).	

SPECIAL NOTES ON OFFICIAL SOLUTIONS

LIQUOR ACIDI ARSENOSI—Solution of Arsenous Acid

(**Liq. Acid. Arsen.**—Hydrochloric Solution of Arsenic—Solution of Arsenic Chloride)

Solution of Arsenous Acid contains, in each 100 cc., the equivalent of not less than 0.975 Gm. and not more than 1.025 Gm. of As_2O_3.

Ingredients.—Arsenic trioxide, 10 Gm.; diluted hydrochloric acid, 50 cc.; distilled water, enough to make 1 liter.

Manipulation.—Dissolve the acid in 250 cc. water; boil the arsenic trioxide therein until it is dissolved. After cooling, add enough water to make 1 liter.

Assay.—See U.S.P., p. 204.

Remarks.—This is an approximately 1 per cent solution of arsenous acid in water, containing 5 per cent of diluted hydrochloric acid. The preparation was formerly called *solution of arsenic chloride,* it being assumed that the hydrochloric acid combined with the arsenous acid with the formation of the chloride. This view is not generally held, however, at the present time. It is presumed to be the function of the hydrochloric acid merely to aid in dissolving the arsenic trioxide.

Dose.—0.2 cc. (3 minims).

LIQUOR AMMONII ACETATIS—Solution of Ammonium Acetate

This useful preparation, known as *Spirit of Mindererus,* will be discussed on p. 503.

LIQUOR CALCII HYDROXIDI—Solution of Calcium Hydroxide

(**Liq. Calc. Hydrox.**—Liquor Calcis, Lime Water)

Solution of Calcium Hydroxide is an aqueous solution containing, in each 100 cc., at 25° C., not less than 0.14 Gm. of $Ca(OH)_2$. The content of calcium hydroxide varies with the temperature at which the solution is stored, being about 0.17 Gm. per 100 cc. at 15° C., and less at a higher temperature.

Storage.—Preserve in well-filled, tightly-stoppered bottles, in a cool place.

Ingredients.—Calcium hydroxide 3 Gm.; distilled water, enough to make 1 liter.

Manipulation.—Add the calcium hydroxide to the cool distilled water and agitate the mixture repeatedly during one hour. After the excess has settled, decant and dispense the clear supernatant liquid.

Description.—A clear, colorless, odorless liquid with alkaline, sweetish taste.

Tests for Identity.—Alkaline to litmus, becomes turbid on heating, absorbs CO_2 from air to form a film of carbonate.

Test for Purity.—Alkalies and their carbonates. See U.S.P., p. 205.

Assay.—See U.S.P., p. 206.

Remarks.—This well-known preparation, commonly called *Lime Water,* was formerly prepared by slaking or hydrating calcium oxide. It is now made from powdered calcium hydroxide. In the present system of grouping pharmaceuticals the old Latin name *Aqua Calcis* is a misnomer, since its active constituent, calcium hydroxide, is a nonvolatile solid, while official waters are solutions of volatile bodies.

Dose.—15 cc. (4 fluidrachms).

LIQUOR CRESOLIS SAPONATUS—Saponated Solution of Cresol

This official, similar to but not identical with the proprietary preparations, *creolin* and *lysol,* will be discussed among the cresol derivatives (p. 791).

LIQUOR EPINEPHRINÆ HYDROCHLORIDI—Solution of Epinephrine Hydrochloride

This solution of epinephrine is discussed on page 817.

LIQUOR ERGOSTEROLIS IRRADIATI—Solution of Irradiated Ergosterol

This solution is discussed on page 957.

LIQUOR FERRI CHLORIDI—Solution of Ferric Chloride

LIQUOR FERRI TERSULFATIS—Solution of Ferric Sulfate

These two chemical solutions of iron will be discussed in the chapter devoted to that element (Chapter XXXI).

LIQUOR FORMALDEHYDI—Solution of Formaldehyde

This 37 per cent solution of formaldehyde in water, sometimes called *Formalin*, will be discussed under Formaldehyde (p. 650).

LIQUOR HEPATIS—Solution of Liver

LIQUOR HEPATIS PURIFICATUS—Purified Solution of Liver

These liver solutions will be discussed on page 966.

LIQUOR HISTAMINÆ PHOSPHATIS—Solution of Histamine Phosphate

This solution will be discussed on page 950.

LIQUOR HYDROGENII PEROXIDI—Solution of Hydrogen Peroxide

This largely used 3 per cent Solution of Hydrogen Peroxide is discussed at length on page 416.

LIQUOR IODI COMPOSITUS—Compound Solution of Iodine
(Liq. Iodi Co.—Lugol's Solution)

Compound Solution of Iodine is a solution containing, in each 100 cc., not less than 4.5 Gm. and not more than 5.5 Gm. of I, and not less than 9.5 Gm. and not more than 10.5 Gm. of KI.

Storage.—Preserve in glass bottles, closed with stoppers resistant to corrosion, and in a cool place, protected from light.

Condensed Recipe.

Dissolve 5 Gm. iodine and 10 Gm. potassium iodide in enough distilled water to make 100 cc.

Description.—Transparent brown liquid.

Test for Identity.—Blues starch paste. For details see U.S.P., p. 214.

Assay.—See U.S.P., p. 214.

Remarks.—The synonym of this compound is *Lugol's solution,* which should not be confounded with *Dobell's solution* (p. 214), as it was in one case when a pharmacist translated the poor writing of a physician calling for Dobell's solution into Lugol's solution, which was accordingly sprayed into the throat, with exceedingly irritating results.

Dose.—0.2 cc. (3 minims).

LIQUOR MAGNESII CITRATIS—Solution of Magnesium Citrate

This popular and valuable official sometimes called "Purgative Lemonade," will be discussed on page 517.

LIQUOR PARATHYROIDEI—Solution of Parathyroid

LIQUOR PITUITARII POSTERII—Solution of Posterior Pituitary

These official solutions will be discussed under the animal products in Chapter LI.

LIQUOR POTASSII ARSENITIS—Solution of Potassium Arsenite

Can best be studied among the derivatives of potassium (Chapter XXV).

LIQUOR SODII HYPOCHLORITIS—Solution of Sodium Hypochlorite

LIQUOR SODII HYPOCHLORITIS DILUTUS—Diluted Solution of Sodium Hypochlorite

These two official chlorinated solutions will be considered in Chapter XXIII.

LIQUOR SODII CHLORIDI PHYSIOLOGICUS—Physiological Solution of Sodium Chloride

(**Liq. Sod. Chlor. Physio.**—Physiological Salt Solution, Normal Saline Solution)

Note.—This Solution must be protected from contamination and should be used within twenty-four hours after its sterilization if not stored in hermetically-sealed containers.

If stored in hermetically-sealed containers, it should conform to the tests for *sterility* on page 469, U.S.P.

Condensed Recipe.

Dissolve 8.5 Gm. sodium chloride in distilled water enough to make 1 liter, free the solution from foreign particles and then sterilize in an autoclave under pressure. For details, see U.S.P., pp. 219 and 220.

Remarks.—This official preparation is furnished in response to a demand for a *normal saline solution* (p. 487). Note that the product must be dispensed in sterile condition (Chap. LII) and must not be used intravenously when more than twenty-four hours old nor for other purposes more than twenty-four hours after sterilization unless it has been stored in hermetically-sealed containers. It should conform to the U.S.P. tests for sterility if stored in hermetically-sealed containers. Some surgeons prefer the *Locke-Ringer Solution* which contains 0.9 per cent of sodium chloride and also the chlorides of potassium, calcium and magnesium, as well as some dextrose. Calcium chloride, magnesium sulfate, and sodium phosphate have also been used in the preparation of such solutions. A recipe for this solution is found in U.S.P. XI, page 553.

Isotonic Solutions.—Normal saline solution and Locke-Ringer's solution are typical illustrations of the now largely used class of *isotonic solutions*. The N.F. VI isotonic solution of dextrose and sodium chloride is an example of an official solution of this character. These are sterile aqueous solutions of salts possessing osmotic pressure similar to the blood serum or other body fluids. They are used to replace serious losses of blood. Among other physical constants that play an important rôle in isotonic solutions are the freezing point and the hydrogen-ion concentration (p. 1034). We have learned above that normal saline solution, intended for intravenous use, should contain about 0.9 per cent sodium chloride. On the other hand, a solution intended as a collyrium should be isotonic with the tear fluid and should therefore contain about 1.4 per cent sodium chloride.

Physiologists are employing different combinations of salts in preparing isotonic solutions, the important factor kept constantly in mind being that the prepared solution must have the same osmotic pressure as the body fluid it is to replace or mix with. Nicola has worked out a mathematical equation showing just how salts of various kinds may be diluted to obtain isotonic solutions. Scoville and also Brown have shown the application of Nicola's equation in the preparation of both hypodermic solutions and of collyria. For details, the reader is referred to the articles cited in the Bibliography, at the end of this chapter.

Liquor Arseni et Hydrargyri Iodidorum (U.S.P. X; N.F. VI) or *Solution of Arsenic and Mercuric Iodides*, also known as *Donovan's Solution*.—Solution of Arsenic and Mercuric Iodides is an aqueous solution containing, in each 100 cc., not less than 0.95 Gm. and not more than 1.05 Gm. of AsI_3, and not less than 0.95 Gm. and not more than 1.05 Gm. of HgI_2. It should be preserved in well-closed glass containers, protected from light. It is made by triturating 10 Gm. each of mercuric and arsenous iodides with water until dissolved, filtering, adding water to 800 cc. and then 9 Gm. of sodium bicarbonate. When effervescence ceases, enough water is added to make 1 liter.

This preparation contains approximately 1 per cent of arsenous iodide and 1 per cent of mercuric iodide dissolved in water. The National Formulary directs that Donovan's solution should be not more than a pale yellow color; but on standing this solution becomes red, and such red solutions should not be dispensed, as it is supposed to contain traces of free iodine. This may be prevented by placing a globule of mercury in the container holding the solution and by following the N.F. direction to store in well-filled amber bottles.

Dose.—0.1 cc. (1½ minims).

Liquor Plumbi Subacetatis Dilutus (U.S.P. IX; N.F. VI) or *Diluted Solution of Lead Subacetate*, is the well-known pharmaceutical and is commonly called *lead water*. It is made by mixing 35 cc. of solution of lead subacetate (N.F. VI) with 965 cc. of recently boiled, distilled water. Recently boiled water is directed to rid the water of its dissolved carbonic acid, for if the unboiled water is brought into contact with the solution of lead subacetate, a precipitation of lead carbonate occurs, with corresponding loss in the lead strength of the preparation. In order to prevent the formation of this lead carbonate the Formulary directs that the solution be kept in small, well-filled, well-stoppered bottles. Lead water is best dispensed opalescent, to avoid the danger of confusing this poisonous preparation with the harmless "lime water." Lead water is used as a soothing wash for frost-bite, ivy poisoning, etc. It is used externally only and undiluted.

Liquor Sodii Arsenatis (U.S.P. IX; N.F. VI) or *Solution of Sodium Arsenate*, is made by dissolving 10 Gm. exsiccated sodium arsenate in distilled water enough to make 1 liter. It must not be confused with *Pearson's Solution of Sodium Arsenate* (N.F. V) which contains only 1 Gm. of exsiccated sodium arsenate in 1000 cc. of solution.

THE DOSES OF OFFICIAL SOLUTIONS

0.1 cc. (1½ minims)	Solutions of arsenic and mercuric iodides (N.F. VI) and ferric chloride.
0.2 cc. (3 minims)	Solutions of arsenous acid, ferric subsulfate (N.F. VI) iodine compound, potassium arsenite and sodium arsenate (N.F. VI).
0.3 cc. (5 minims)	Solutions of irradiated ergosterol and potassium iodide (N.F. VI).
0.3 cc. (5 minims) (parenterally)	Solution of histamine phosphate.
0.5 cc. (8 minims) (parenterally)	Solution of epinephrine hydrochloride.
1 cc. (15 minims)	Solution of potassium hydroxide (N.F. VI).
1 cc. (15 minims) (hypodermically)	Solutions of posterior pituitary and procaine hydrochloride (N.F. VI).
4 cc. (1 fluidrachm)	Solution of hydrogen peroxide.

8 cc. (2 fluidrachms)	Solutions of peptonized iron (N.F. VI), peptonized iron and manganese (N.F. VI), soda and mint (N.F. VI), sodium citrate (N.F. VI) and sodium phosphate (N.F. VI).
15 cc. (4 fluidrachms)	Solutions of ammonium acetate, calcium hydroxide, iron and ammonium acetate (N.F. VI) and potassium citrate (N.F. VI).
200 cc. (7 fluidounces)	Solution of magnesium citrate.
1000 cc. (33.8 fluidounces) intravenously	Isotonic solution of dextrose and sodium chloride (N.F. VI).
0.5 to 4 cc. (8 minims to 1 fluidrachm) based on the weight of the animal	Solution of nux vomica alkaloids (N.F. VI).
Average dose to be stated upon the label of the container	Solutions of liver and liver purified.
25 units hypodermically	Solution of parathyroid.

No doses are assigned the official solutions not mentioned in the above list.

THE SOLUTIONS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Liquor acidi borici.	Saturated solution of boric acid.	Boric acid, 50 Gm.; distilled water.	
Liquor alumini acetatis.	Burow's solution.	Lead acetate; aluminum sulfate; water.	See p. 548
Liquor alumini chloridi.	Solution of aluminum chloride.	Aluminum chloride, 250 Gm ; water.	
Liquor alumini subacetatis.	Solution of aluminum subacetate.	Aluminum sulfate; acetic acid, precipitated calcium carbonate; water.	Largely used by German practitioners (p. 548).
Liquor amaranthi.	Solution of amaranth	Amaranth; distilled water.	Coloring agent.
Liquor antisepticus.	Antiseptic solution	Boric acid, 25 Gm ; thymol; chlorthymol; eucalyptol, methyl salicylate; oil of thyme; menthol; alcohol; water. Purified talc as clarifier.	For external or oral use; undiluted.
Liquor aromaticus alkalinus.	Alkaline aromatic solution	Potassium bicarbonate, 20 Gm.; sodium borate, 20 Gm.; thymol, eucalyptol; methyl salicylate; alcohol; glycerin water. Cudbear as color and talc as clarifier.	An agreeable product similar to the many proprietary products now on the market.
Liquor arseni et hydrargyri iodidorum.	Donovan's solution.	Arsenic triiodide, 10 Gm.; red mercuric iodide, 10 Gm ; sodium bicarbonate; distilled water	
Liquor calcis sulfuratæ.	Vleminckx' solution.	Lime, 165 Gm.; sublimed sulfur, 250 Gm ; water.	See p. 430.
Liquor carmini	Solution of carmine.	Carmine, 65 Gm.; ammonia water; glycerin; distilled water.	Valuable coloring agent.
Liquor cocci.	Cochineal color.	Cochineal, 65 Gm.; potassium carbonate; alum; potassium bitartrate; glycerin; distilled water.	Another valuable coloring agent.
Liquor dextrosi et sodii isotonici.	Isotonic dextrose-saline solution.	Dextrose; physiological solution of sodium chloride; freshly distilled water.	
Liquor ephedrinæ sulfatis.	Solution of ephedrine sulfate.	Ephedrine sulfate; chlorobutanol; distilled water.	
Liquor ferri et ammonii acetatis.	Basham's mixture.	Tincture of ferric chloride; diluted acetic acid; solution of ammonium acetate; aromatic elixir; glycerin; distilled water.	
Liquor ferri peptonati.	....	....	These two preparations as well as solution of albuminate of iron are discussed in Chapter LI.
Liquor ferri peptonati et mangani.	....	....	

THE SOLUTIONS OF THE NATIONAL FORMULARY—(*Continued*)

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Liquor ferri subsulfatis.	Monsel's solution.	Ferrous sulfate; sulfuric acid; nitric acid (as oxidizer); distilled water.	See p. 570.
Liquor iodi phenolatus.	Boulton's solution.	Compound solution of iodine, 15 cc.; liquefied phenol, 6 cc.; glycerin; water.	See p. 773.
Liquor methylrosanilini.	Solution of crystal, methyl or gentian violet.	Methyl-rosaniline, 30 Gm.; alcohol; water.	Coloring agent.
Liquor nucis vomicæ alkaloidorum.	Nux alkaloids solution.	Brucine sulfate, 16 Gm.; strychnine sulfate, 16 Gm.; glycerin; caramel; distilled water.	Veterinary preparation.
Liquor picis carbonis.	Coal tar solution.	Coal tar 200 Gm.; quillaja; alcohol.	A popular dermatological preparation.
Liquor plumbi subacetatis.	Goulard's extract	Lead acetate; lead monoxide; distilled water.	See p. 606.
Liquor plumbi subacetatis dilutus.	Lead water.	.. ..	See p. 607.
Liquor potassii citratis.	Solution of potassium citrate.	Potassium bicarbonate; citric acid; distilled water.	
Liquor potassii hydroxidi.	Solution of potassium hydroxide.	Potassium hydroxide; distilled water.	*Dose*—1 cc (15 minims), freely diluted with water before being taken into the mouth.
Liquor potassii iodidi.	Saturated solution of potassium iodide.	Potassium iodide, 1000 Gm.; sodium thiosulfate, 0.5 Gm; distilled water	See p. 470.
Liquor procainæ hydrochloridi.	Dental anesthetic solution.	Procaine hydrochloride, 20 Gm.; physiological solution of sodium chloride.	Used hypodermically with epinephrine solution.
Liquor sodæ et menthæ.	Soda mint.	Sodium bicarbonate; aromatic spirit of ammonia; spearmint water.	*Dose.*—8 cc. (2 fluidrachms).
Liquor sodii arsenatis.	Solution of sodium arsenate.	. . . .	See p.584.
Liquor sodii boratis compositus.	Dobell's solution.	Sodium borate; sodium bicarbonate; liquefied phenol; glycerin; distilled water.	Used as a nasal douche
Liquor sodii citratis.	Potio Riverii.	Citric acid; sodium bicarbonate; distilled water	*Dose*—8 cc (2 fluidrachms). See p. 468.
Liquor sodii phosphatis.	....	Sodium phosphate, 400 Gm.; citric acid, glycerin; distilled water.	See p. 489.

AMPULLÆ

This is a special class of sterile solutions dispensed in ampuls. The National Formulary gives a General Monograph on *ampullæ* and also recipes for 28 specific ampul solutions. These will be discussed in Chapter LII.

COLLYRIA

These are special types of solutions recognized in some of the European pharmacopœias intended for use as eye washes. A typical illustration is *collyrium adstringens luteum* of the Austrian pharmacopœia, the formula for which will be found in the A.Ph.A. Recipe Book. *Gifford's Solution* is a type of collyrium carefully adjusted to the proper hydrogen-ion concentration. It consists of an acid solution, 12.4 Gm. of boric acid, 7.4 Gm. of potassium chloride and enough distilled water to make 1000 cc. and an alkali solution consisting of 21.2 Gm. of anhydrous sodium carbonate and distilled water to make 1000 cc. By mixing appropriate volumes of these two solutions, collyria of *p*H 5 to *p*H 9 may be obtained.

In dispensing collyria great care should be taken that the finished product is free from foreign particles. The filtration is best done through sterile absorbent cotton.

A number of special bottles have been devised for dispensing collyria. Collunaria, nasal douches or "nose drops" are discussed on page 293.

MUCILAGES

The mucilages are *aqueous preparations containing viscid substances in solution or suspension*, and from a strictly physical point of view mucilages should scarcely be grouped among the solutions.

All mucilages should be freshly prepared, as their mucilaginous constituents when diluted with water are usually prone to fermentation.

One of the official mucilages is a jelly and the other is a liquid. One is prepared with hot water; the other with cold water. Both are galenic preparations.

SPECIAL NOTES ON OFFICIAL MUCILAGES

MUCILAGO ACACIÆ—Mucilage of Acacia
(Mucil. Acac.—Mucilage of Gum Arabic)

Caution.—Mucilage of Acacia must not be dispensed if it has become sour or moldy.

Condensed Recipe.

Dissolve 350 Gm. acacia (previously washed in cold water) in warm distilled water enough to make 1000 Gm., agitating the mixture in a graduated bottle until solution is effected. One Gm. sodium benzoate is added as a preservative. For details, see U.S.P., p. 238.

Remarks.—This preparation contains 35 per cent of washed gum arabic dissolved in water, and the Pharmacopœia directs that the gum arabic be in the form of small pieces and not in a powder. For general prescription purposes, however, especially when the mucilage of gum arabic is directed as one of the several ingredients, the powdered gum arabic is generally used in the act of dissolving; it being much quicker than when gum arabic in lumps is employed.

In preparing large quantities of the mucilage of acacia, as in making mucilage to sell as an adhesive, the solution of the gum can be facilitated by placing it in a muslin bag and suspending it on the surface of the water contained in the crock. In this way the gum arabic can be easily dissolved in the course of a few hours by means of a circulatory solution.

Dose.—15 cc. (4 fluidrachms).

MUCILAGO TRAGACANTHÆ—Mucilage of Tragacanth
(Mucil. Trag.)

Condensed Recipe.

Ingredients.—Tragacanth, 6 Gm.; glycerin, 18 Gm.; water enough to make 100 Gm.

Manipulation.—Mix the glycerin with 75 cc. of water, heat to boiling, add the tragacanth, macerate twenty-four hours. Then add the full amount of water and strain by expression. For details, see U.S.P., p. 239.

Remarks.—This mucilage is prepared by adding tragacanth to boiling water mixed with glycerin and straining after maceration for twenty-four hours. The glycerin aids in its preservation. It is a semisolid of much value as a pill excipient, and is practically never used internally.

Mucilago Chondri (N.F. VI) or *Mucilage of Chondrus*, also known as *Mucilage of Irish Moss*, is the only mucilage listed in the N.F. VI. It is made by washing 3 Gm. of chondrus with cold water, and then heating with 100 cc. of boiling water on a water bath and straining. This mucilage is used in making emulsions.

Mucilago Ulmi (U.S.P. VIII) was prepared by digesting 6 Gm. of elm bark in 100 mils of water for one hour, after which it was strained.

Mucilago Sassafras Medullæ (N.F. V) or *Mucilage of Sassafras Pith* is prepared by cold infusion and is used as the vehicle in eye lotions.

SYRUPS

The next class of preparations to claim our attention are the syrups, which are *preparations containing medicated or flavoring substances combined with a concentrated aqueous solution of sucrose,* previously referred to as saccharum or sugar.

A concentrated aqueous solution of sucrose is called *syrup* or simple syrup. If the substance added to this is merely a pleasant fruit or an aromatic, the finished product is a *flavored syrup,* while if the addition is of a medicinal character, the product is a *medicated syrup.*

The manufacture of syrups, while it is simple in each individual case, is rather difficult to explain in a general way by reason of the many modifications in the several processes directed in the Pharmacopœia. Moreover, the manufacture of the syrups may be considered from two points of view: first, the method by which the sucrose is dissolved, and second, the method in which the medicinal or flavoring constituent is blended with the sucrose.

As far as dissolving the sucrose is concerned, this is accomplished in several ways: first, the *solution of sucrose with heat,* that is, by placing the sugar in an appropriate vessel, adding water, and possibly a medicated liquid, and warming the mixture until the sucrose is dissolved. The second method is by dissolving the sucrose in a medicated liquid without the use of heat—the so-called *cold process* of preparing syrups. This process must, in turn, be divided into two methods, the sucrose being dissolved in the first case by *agitation* (by simply mixing the sucrose with the medicated liquid, and shaking the container from time to time until the sucrose is completely dissolved), and in the second case, by *percolation.* In this method a piece of sponge or large pledget of absorbent cotton is put in the neck of the percolator, the granulated sucrose is poured thereon and packed down as well as circumstances permit, and the requisite amount of the liquid is poured upon it. The liquid is attracted downward by the force of gravitation, and in traversing through the sugar dissolves enough of it to make a saturated solution; and in this way, if the requisite quantity of liquid is added, all the sucrose will be dissolved, and at the end of the process nothing will remain in the percolator except the straining medium and any insoluble matter that was mixed with the sucrose.

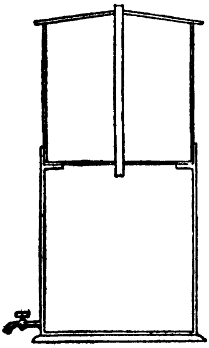


Fig. 188.—Syrup percolator.

For preparing pharmacopœial syrups this process of percolation is permitted, but the writer has found that it possesses the great objection that there is always a considerable quantity of sucrose which is not dissolved by the percolating liquid, and in order to redissolve this it is necessary to spread the sugar carefully over the cotton plug and pass the liquid through once more. But even this is not always successful.

For the preparation of syrup for soda-fountain use this method of cold percolation is unexcelled, for in this case the complete solution of the sucrose is not absolutely necessary. Soda syrup can be prepared in the very simple apparatus shown in Fig. 188. This apparatus was built of 2 5-gallon tins, the lower one provided with a brass faucet, while a sufficient amount of the bottom of the upper one was left to form a margin on which rested a diaphragm of tinned iron, pierced with holes, over which was placed a piece of Canton flannel which served as a strainer.

TABLE OF OFFICIAL SYRUPS

Process	*Galenic Preparations*	*Chemical Preparations*
Adding Medicated Liquid to a Syrup. *Medicating Liquid.*		
Aqueous solution.	Syrup of ammonium hypophosphite (N.F. VI).	
	Syrup of citric acid.	
	Syrup of ephedrine sulfate (N.F. VI).	
	Syrup of potassium guaiacolsulfonate (N.F. VI)	
	Syrup of white pine, compound with morphine (N.F. VI).	
Fluidextract.	Syrup of glycyrrhiza (N.F. VI).	
	Syrup of ipecac.	
	Syrup of rhubarb (N.F. VI).	
	Syrup of sarsaparilla, compound.	
	Syrup of senega (N.F. VI).	
Oil.	Syrup of cinnamon (N.F. VI).	
Tincture.	Syrup of ipecac and opium (N.F. VI).	
	Syrup of rhubarb, aromatic.	
Dissolving Sucrose in the Medicating Liquid. *Medicating Liquid.*		
Aromatic water.	Syrup of orange flowers.	
Aqueous extract.	Syrup of althea (N.F. VI).	
Aqueous mixture.	Syrup of prepared cacao (N.F. VI).	
Aqueous solution.	Syrup of acacia (N.F. VI).	Syrup of ferrous iodide.
	Syrup of the bromides (N.F. VI).	
	Syrup of hydriodic acid.	Syrup of calcium lactophosphate (N.F. VI).
	Syrup of hypophosphites (N.F. VI).	
	Syrup of hypophosphites, compound (N.F. VI).	
	Syrup of pine tar.	
Fruit juice.	Syrup of cherry (N.F. VI).	
	Syrup of raspberry (N.F. VI).	
Diluted fluidextract.	Syrup of eriodictyon, aromatic (N.F. VI).	
	Syrup of ginger (N.F. VI).	
	Syrup of senna.	
	Syrup of squill, compound (N.F. VI).	
	Syrup of thyme (N.F. VI).	
	Syrup of trifolium, compound (N.F. VI).	
Percolate.	Syrup of asarum, compound (N.F. VI).	
	Syrup of wild cherry.	
	Syrup of white pine, compound (N.F. VI).	
Diluted tincture.	Syrup of orange.	
	Syrup of tolu balsam.	
Vinegar.	Syrup of squill.	

Through the center of this diaphragm, up to the top of the upper can, passes a piece of tin tubing intended to permit the exit of air from the lower can. This diaphragm being placed in position, granulated sucrose is thrown in the upper can until completely filled, and 1 gallon of water is poured thereon. The water penetrates the sugar, dissolving it, and is finally passed through the strainer on the diaphragm, dropping into the lower can a saturated solution of sucrose in water. When the first gallon of water has passed through the sucrose is repacked in the upper can, and a ½-gallon of water poured on; and we thus obtain about 4 to 5 gallons of a thick, transparent syrup. The sucrose remaining in the upper can is poured on paper, dried, and used another time with a fresh quantity of sucrose. The quality of the sucrose used in making syrups is of great importance, as some brands of sucrose give syrup that does not keep well. "Crystal A" confectioners' sugar is the one recommended.

As to the special methods of manufacturing syrups, the table on page 217 gives a glance at the various processes employed in making all official syrups except Syrup U.S.P.

The table affords an insight into the many modifications necessary in preparing the official syrups, and we can now turn to a special consideration of the points regarding the official syrups, giving the same in alphabetic order.

SPECIAL NOTES ON OFFICIAL SYRUPS

SYRUPUS—Syrup

(Syrup—Simple Syrup)

Storage.—Preserve in well-closed containers in a cool place.

Condensed Recipe.

Dissolve 850 Gm. sucrose in enough distilled water to make 1 liter, either by hot solution or by cold percolation. The amount of water used at first in either method is 450 cc. For details, see U.S.P., p. 371.

Remarks.—Syrup, or what is commonly called *simple syrup,* is approximately a 65 per cent solution of sucrose in water. In 1000 cc. (or 1313 Gm.) of the syrup there are 850 Gm. of sucrose dissolved, hence the percentage strength is 850 ÷ 1313 or 64.7. It is prepared either by dissolving by boiling with water or by percolation of water through sucrose. The official syrup should have a specific gravity of about 1.313, and it is exceedingly poor economy to attempt to use a syrup much thinner than this. Syrups containing a smaller quantity of sucrose will invariably ferment, and the apparent economy in saving a small quantity of sucrose in making the syrup is more than counterbalanced by the necessity of throwing away a batch of spoiled syrup. If the syrup is properly prepared, there is no necessity for elaborate precautions of preserving the same, although it should, of course, be kept in well-stoppered bottles. Forch has studied the keeping qualities of simple syrup and other pharmacopœial syrups and has found that when properly prepared and stored the bacterial count is insignificant.

Mayer and also Kebler find that the sucrose, however, is quickly inverted into dextrose and levulose.

Sturmer has recently pointed out that syrup is frequently a better solvent for salts than is water.

SYRUPUS ACIDI CITRICI—Syrup of Citric Acid

(Syr. Acid. Cit.)

Condensed Recipe.

Ingredients.—Citric acid, 10 Gm.; distilled water and tincture of lemon, of each, 10 cc.; syrup, enough to make 1 liter.

Manipulation.—Dissolve the acid in the water and add to the syrup. Then add the tincture and enough syrup to make a liter. For details, see U.S.P., p. 372.

Remarks.—This is approximately the average soda-fountain syrup of lemon, although that made from the fresh lemons is much to be preferred. Used entirely as a flavor. No dose given by the Pharmacopœia.

SYRUPUS ACIDI HYDRIODICI—Syrup of Hydriodic Acid

This official derivative of hydriodic acid can best be explained in Part III (p. 444).

SYRUPUS AURANTII—Syrup of Orange

(Syr. Aurant.)

Condensed Recipe.

Ingredients.—Tincture of sweet orange peel, 50 cc.; citric acid, 5 Gm.; sucrose, 820 Gm.; distilled water enough to make 1 liter. Purified talc as clarifier.

Manipulation.—Triturate the talc with the tincture and the acid and add 400 cc. of water, filter, dissolve the sucrose in the filtrate, without heat and finally add enough water to make a liter. For details, see U.S.P., p. 373.

Remarks.—This is a very palatable flavoring syrup, hence no dose is assigned it in the Pharmacopœia.

SYRUPUS AURANTII FLORUM—Syrup of Orange Flowers

(Syr. Aurant. Flor.)

Condensed Recipe.

Dissolve 850 Gm. sucrose in a mixture of 225 cc. orange flower water and an equal amount of distilled water, either by agitation or by percolation. Then add enough water to make 1 liter. For details, see U.S.P., p. 373.

Remarks.—Another pleasant flavoring syrup.

SYRUPUS BALSAMI TOLUTANI—Syrup of Tolu Balsam

(**Syr. Balsam. Tolu.**—Syrupus Tolu U.S.P. X, Syrup of Tolu)

Condensed Recipe.

Fifty cc. of tincture of tolu balsam are triturated with 10 Gm. magnesium carbonate, 60 Gm. sucrose and with 430 cc. distillated water. The mixture is filtered and 760 Gm. sugar are dissolved in the filtrate by aid of gentle heat. The syrup is strained and the strainer is then washed with enough water to make 1 liter. The sucrose may also be dissolved in the filtrate by cold percolation. For details, see U.S.P., p. 374.

Remarks.—The official recipe just given is substantially the process of the Pharmacopœia of 1870, and yields a handsome aromatic yellow syrup. The process of 1880—digesting a mixture of balsam of tolu and sucrose with water—was cumbersome and yielded a poor product, and the process of 1890—dissolving sucrose in a water of tolu made by rubbing an alcoholic solution of the balsam with precipitated calcium phosphate and water—was not much better. The color is due to the fact that the alkaline magnesium carbonate acts on the resin of the balsam found in the tincture, producing a characteristic yellow tint.

Dose.—10 mils (2½ fluidrachms).

SYRUPUS FERRI IODIDI—Syrup of Ferrous Iodide

Fully described among the compounds of iron (Chapter XXXI).

SYRUPUS IPECACUANHÆ—Syrup of Ipecac

(Syr. Ipecac.)

Condensed Recipe.

Ingredients.—Fluidextract of ipecac, 70 cc.: glycerin, 100 cc.; syrup enough to make 1 liter.

Manipulation.—Mix the fluidextract with the glycerin and then add the syrup. For details, see U.S.P., p. 376.

Remarks.—Note that some syrups are made from the fluidextract. There are two processes of making them, one is by simply mixing the fluidextract with the syrup, while in the other fluidextracts are mixed with water and other ingredients, then filtered and the filtrate is used to dissolve the sucrose. The latter process—shown in the recipe for syrup of senna—is much preferable to merely mixing the fluidextract with syrups, which almost invariably yields a cloudy, unsightly product.

Dose.—Expectorant, 0.75 cc. (12 minims). Emetic, 15 cc. (4 fluidrachms).

SYRUPUS PICIS PINI—Syrup of Pine Tar

(Syr. Pic. Pin. Syrupus Picis Liquidæ, Syrup of Tar)

Condensed Recipe.

Ingredients.—Rectified oil of tar, 1 cc.; sucrose, 850 Gm.; water, enough to make 1 liter.

Manipulation.—Shake and macerate the oil with distilled water during twenty-four hours, then filter and dissolve the sucrose in the filtrate. For details, see U.S.P., p. 376.

Remarks.—While U.S.P. IX directed the manufacture of this syrup from tar, U.S.P. X and XI direct use of oil of tar, thus simplifying manipulation.

SYRUPUS PRUNI VIRGINIANÆ—Syrup of Wild Cherry

(Syr. Prun. Virg.)

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Condensed Recipe.

Ingredients.—Wild cherry bark, 150 Gm.; sucrose, 800 Gm.; glycerin, 50 cc.; alcohol, 20 cc.; distilled water, enough to make 1 liter.

Manipulation.—Percolate the powdered bark with a mixture of glycerin and distilled water. Add the alcohol to the percolate and dissolve the sucrose therein by cold agitation. For details, see U.S.P., p. 377.

Remarks.—This syrup, which enjoys just popularity, is made by percolating wild cherry bark with a cold mixture of glycerin and water; dissolving sugar in the percolate thus obtained. The alcohol is added as a preservative. This is a medicated syrup and must not be confused with Syrup of Cherry N.F. which is designed purely as a flavoring agent.

It is imperative that heat be avoided in making this syrup, since heat prevents the formation or causes the volatilization of the active principle, hydrocyanic acid. (See p. 795.) Kebler claims, however, that the amount of hydrocyanic acid in the syrup is negligible.

Dose.—10 cc. (2½ fluidrachms).

SYRUPUS RHEI AROMATICUS—Aromatic Syrup of Rhubarb

(Syr. Rhei Arom.—Spiced Syrup of Rhubarb)

Condensed Recipe.

Dissolve 1 Gm. potassium carbonate in 150 cc. aromatic tincture of rhubarb and then add enough syrup to make 1 liter.

Remarks.—This syrup is made by mixing syrup with aromatic tincture of rhubarb, previously rendered alkaline with potassium carbonate. The alkali is employed for the same reason as in making syrup of rhubarb. Turn to aromatic tincture of rhubarb (p. 251), and note what aromatics it contains.

Dose.—10 cc. (2½ fluidrachms).

SYRUPUS SARSAPARILLÆ COMPOSITUS—Compound Syrup of Sarsaparilla

(Syr. Sarsap. Co.)

Condensed Recipe.

Ingredients.—Fluidextract of sarsaparilla, 200 cc.; fluidextract of glycyrrhiza, 15 cc.; oils of sassafras and anise, of each 0.2 cc.; methyl salicylate, 0.2 cc.; alcohol; syrup enough to make 1 liter.

Manipulation.—Dissolve the oils in the alcohol, add the fluidextracts and then mix with the syrup. For details, see U.S.P., p. 378.

Remarks.—*Compound syrup of sarsaparilla* affords a good test of memory, and its constituents form a question of which some examining boards were quite fond. Note the two fluidextracts and the three oils used in its manufacture. The uses of the syrup as an adjuvant, especially for quinine, are well known.

Dose.—15 cc. (4 fluidrachms).

SYRUPUS SCILLÆ—Syrup of Squill

(Syr. Scill.)

Condensed Recipe.

Dissolve 800 Gm. sucrose in 450 cc. vinegar of squill by gentle heat and finally add enough distilled water to make 1 liter.

Remarks.—Syrup of squill is now made by dissolving sucrose in vinegar of squill at gentle heat. In the Pharmacopœia of 1890 the vinegar of squill was first boiled and filtered; this is not now necessary, since the boiling is performed in the manufacture of the official vinegar. (See p. 277.)

Dose.—2 cc. (30 minims).

SYRUPUS SENNÆ—Syrup of Senna

(Syr. Senn.)

Condensed Recipe.

Five cc. of oil of coriander are mixed with 250 cc. of fluidextract of senna and with distilled water. After agitation and maceration during twenty-four hours, the mixture is filtered and 635 Gm. sucrose are dissolved in the filtrate. Lastly enough water is added to make 1 liter. For details, see U.S.P., p. 379.

Remarks.—Note that the National Formulary no longer gives recipes for an *aromatic syrup of senna*; nor for *compound syrup of figs*, both of which contain senna. Recipes for these will be found in the N.F. V.

Dose.—8 cc. (2 fluidrachms).

Syrupus Zingiberis (N.F. VI) or *Syrup of Ginger* is prepared by dissolving 30 cc. of fluidextract of ginger in 20 cc. of alcohol and the solution is triturated with 10 Gm. magnesium carbonate, 60 Gm. sucrose and with water. The mixture is filtered and 760 Gm. sucrose are dissolved in the filtrate as in making syrup of tolu.

Dose.—10 mils (2½ fluidrachms).

Syrupus Rhei (U.S.P. X; N.F. VI) or *Syrup of Rhubarb* is prepared by the addition of fluidextract of rhubarb and spirit of cinnamon, mixed with a solution of potassium carbonate, to syrup. The carbonate aids in dissolving resins found in rhubarb. This syrup is laxative while aromatic syrup of rhubarb is chiefly astringent due to its content of aromatics. *Dose.*—10 cc. (2½ fluidrachms).

Syrupus Scillæ Compositus (U.S.P. X; N.F. VI), also known as *Coxe's Hive Syrup* is made from the fluidextracts of squill and senega. The aqueous solution of the active principles of these drugs and a solution of tartar emetic is filtered after mixing and standing twelve hours and sucrose is dissolved in the resultant filtrate. *Dose.*—2 cc. (30 minims).

Syrupus Senegæ (U.S.P. X; N.F. VI) or *Syrup of Senega* is made by adding syrup to a mixture of fluidextract of senega and ammonia water. Fluidextract of senega contains pectin and ammonia water is used in the recipe to prevent precipitation of the pectin, which would mar the appearance of the syrup. (See p. 270.) *Dose.*—4 cc. (1 fluidrachm).

Syrupus Acaciæ (U.S.P. IX; N.F. VI) or *Syrup of Acacia* is prepared by making a hot solution of 100 Gm. of acacia in 425 cc. of distilled water and dissolving therein 800 Gm. of sucrose. Sodium benzoate is added as a preservative and tincture vanilla is added as a flavor. Thus prepared the product will ferment unless it is stored in small, tightly-stoppered sterile bottles. This syrup is sometimes used as a pill excipient although the pills so made are usually too hard.

Syrupus Amygdalæ (U.S.P. VIII) was prepared by mixing together 10 cc. of spirit of bitter almond, 100 cc. of orange flower water and 890 cc. of syrup. This transparent preparation is quite different from the syrup of almond of the Pharmacopœia of 1890, which was a milky liquid prepared from an emulsion of almond. The latter is popular as a flavor in the South under the name *orgeate syrup.*

Syrupus Ferri, Quininæ et Strychninæ Phosphatum (U.S.P. VIII) is commonly called *Easton's syrup* and is an excellent tonic, although of rather limited popularity because of its intensely bitter taste. To make a stable preparation is a matter of difficulty, the usual product turning black and eventually precipitating. The dose is 4 cc. (1 fluidrachm), containing about $\frac{1}{80}$ grain of strychnine.

Syrupus Hypophosphitum (U.S.P. IX; N.F. VI) or *Syrup of Hypophosphites* is made by dissolving the hypophosphites of calcium (35 Gm.) potassium (18 Gm.) and sodium (18 Gm.) in 500 cc. water and then adding to the solution hypophosphorous acid (1 cc.). This solution is then filtered after which glycerin (50 cc.) and sucrose (600 Gm.) are added and enough distilled water to make 1000 cc. of syrup. In the manufacture of this syrup, if any difficulty is found in dissolving the calcium hypophosphite, the fault is apt to lie in the salt, as a large amount of commercial calcium hypophosphite is not pure. *Dose.*—8 cc. (2 fluidrachms).

Syrupus Hypophosphitum Compositus (U.S.P. VIII; N.F. VI) is a combination of the hypophosphites of calcium, potassium, sodium, iron and manganese along with quinine and strychnine. It is given in doses of 8 cc. (2 fluidrachms).

Syrupus Lactucarii (U.S.P. IX) or *Syrup of Lactucarium,* is made by dissolving 1 Gm. of citric acid in 50 cc. of orange flower water, adding to this a mixture of 100 cc. of tincture of lactucarium and 200 cc. of glycerin and, after filtration adding enough syrup to make 1 liter. A French proprietary form of this preparation enjoyed large vogue as a sedative in coughs until it was found that the real sedative action resided in the morphine which it contained. *Dose.*—10 cc. (2½ fluidrachms).

Syrupus Rosæ (U.S.P. VIII; N.F. V) is made by diluting fluidextract of rose with diluted sulfuric acid and water and then dissolving sucrose in the filtered fluid. It is used as a flavor.

Syrupus Calcii Iodidi (N.F. V) is prepared by first making a solution of ferrous iodide from iodine and iron wire and then treating this with precipitated calcium carbonate, when a solution of calcium iodide is obtained. In this sucrose is dissolved. *Dose.*—2 cc. (30 minims).

Syrupus Iodotannicus (N.F. V) is prepared by heating tannic acid, iodine and water in a flask provided with an upright condenser until the free iodine has become chemically combined with the other ingredients; then sucrose is added. Power claims that the product is nothing else but an impure hydriodic acid. *Dose.*—4 cc. (1 fluidrachm).

Syrupus Pini Albæ Compositus (with and without morphine). The National Formulary recognizes this popular cough remedy both with and without morphine; the former representing the latter, plus 0.4 Gm. of morphine sulfate to the liter. *Syrupus Pini Albæ Compositus* is prepared by percolating white pine bark, wild cherry, spikenard root, poplar buds, sanguinaria, sassafras bark and cudbear with a menstruum composed of glycerin, alcohol and water. In the percolate are dissolved sugar, and chloroform (6 cc. to the liter). The alcohol content is approximately 100 cc. to the liter. The dose of both syrups is 4 cc. (1 fluidrachm).

Syrupus Rubi Idæi (N.F. VI) is the pleasant flavoring syrup of raspberry and the recipe given, like that of the pharmacopœia of 1890, directs that the syrup be prepared from the fresh fruit and not from the commercial fruit juice. The recipe should be read since it is a type formula which can be used for making most of the fruit syrups.

THE SYRUPS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Syrupus acaciæ.	Syrup of acacia.	Acacia, 100 Gm.; sodium benzoate, tincture of vanilla; sucrose; distilled water.	Keep in well closed containers in a cool place.
Syrupus althææ.	Syrup of marshmallow.	Althea root; distilled water; alcohol, 30 cc.; glycerin, 100 cc.; sugar.	Keep in well-stoppered completely filled bottles in a cool place.
Syrupus ammonii hypophosphitis.	Syrup of ammonium hypophosphite.	Ammonium hypophosphite, 35 Gm.; hypophosphorous acid, distilled water, glycerin, syrup.	*Dose.*—4 cc. (1 fluidrachm).
Syrupus asari compositus.	Compound syrup of Canada snake root.	Asarum; potassium carbonate; alcohol; water. Add to the tincture, fluidextract of ipecac; solution of cochineal and sucrose.	Used in whooping cough. Used as vehicle for iodides.
Syrupus bromidorum.	Syrup of the bromides.	Bromides of potassium, sodium, ammonium, calcium, lithium; compound syrup of sarsaparilla; sucrose; distilled water. Tincture of vanilla as flavor, compound tincture of cudbear as color.	*Dose.*—4 cc. (1 fluidrachm).
Syrupus cacao præparati.	Syrup of chocolate.	Prepared cacao; theobroma oil; starch; sucrose; distilled water. Tincture of vanilla as flavor.	A pleasantly flavored syrup.
Syrupus calcii lactophosphatis.	Syrup of calcium lactophosphate.	....	*Dose*—10 cc (2½ fluidrachms). A preparation of U. S. P. IX. See p. 528.
Syrupus cerasi.	Syrup of cherry	The juice of sour cherries, benzoic acid, sucrose, alcohol.	Keep in well closed containers.
Syrupus cinnamomi.	Syrup of cinnamon.	Oil of cinnamon, syrup, compound tincture of cudbear as color.	Keep in well closed containers in a cool place.
Syrupus ephedrinæ sulfatis.	Syrup of ephedrine sulfate.	Ephedrine sulfate, 4 Gm., distilled water; alcohol; syrup of cherry.	*Dose.*—4 cc. (1 fluidrachm).
Syrupus eriodictyi aromaticus.	Syrupus corrigens.	Fluidextract of eriodictyon; solution of potassium hydroxide; compound tincture of cardamom; oils of sassafras, lemon and clove; alcohol; distilled water, magnesium carbonate. Dissolve sucrose in the filtrate	Used as a masker of the bitterness of quinine (see p. 917). *Dose*—8 cc. (2 fluidrachms).
Syrupus glycyrrhizæ.	Syrup of licorice.	Oil of fennel; anethol; benzaldehyde; fluidextract of glycyrrhiza; syrup	A pleasant vehicle for bitter substances.
Syrupus hypophosphitum.	Syrup of hypophosphites.	....	A preparation of U. S.P. IX. See p. 222.
Syrupus hypophosphitum compositus.	....	....	See p. 222.
Syrupus ipecacuanhæ et opii.	Syrup of Dover's powder.	Tincture of ipecac and opium, 85 cc.; spirit of cinnamon; syrup.	*Dose*—4 cc. (1 fluidrachm).
Syrupus pini albæ compositus.	....	....	See p. 222.
Syrupus pini albæ compositus cum morphina.	Compound syrup of white pine with and without morphine.	....	
Syrupus potassii guaiacolsulfonatis.	Syrup of potassium guaiacolsulfonate.	Potassium guaiacolsulfonate, 75 Gm.; distilled water; aromatic syrup of eriodictyon.	*Dose.*—4 cc. (1 fluidrachm).
Syrupus rhei.	Syrup of rhubarb.	Fluidextract of rhubarb; spirit of cinnamon; potassium carbonate; distilled water; syrup.	*Dose.*—10 cc. (2½ fluidrachms); potassium carbonate aids solutions of the resins found in rhubarb.

THE SYRUPS OF THE NATIONAL FORMULARY—(*Continued*)

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Syrupus rubi idæi.	... .	Raspberry juice; sucrose; benzoic acid; alcohol.	See p. 222.
Syrupus scillæ compositus.	Hive syrup; Coxe's hive syrup.	Fluidextracts of squill and senega, antimony and potassium tartrate; sucrose; distilled water.	*Dose.*—2 cc. (30 minims).
Syrupus senegæ.	Syrup of senega.	Fluidextract of senega, 200 cc.; ammonia water; syrup	*Dose.*—4 cc. (1 fluidrachm).
Syrupus thymi.	Syrup of thyme.	Fluidextract of thyme, 200 cc.; sucrose, distilled water; magnesium carbonate as filtering agent.	
Syrupus trifolii compositus.	Compound syrup of trifolium.	Compound fluidextract of trifolium, 300 cc.; powdered tragacanth; oils of sassafras and anise; methyl salicylate, sucrose; distilled water.	The oils are emulsified by use of the tragacanth and the mixture then made into a syrup. *Dose.*—8 cc (2 fluidrachms)
Syrupus zingiberis.	Syrup of ginger.	Fluidextract of ginger, 30 cc.; alcohol magnesium carbonate; sucrose; distilled water.	*Dose*—10 cc (2½ fluidrachms)

Syrupus Sennæ Aromaticus (N.F. V) is prepared by percolating jalap, rhubarb, cinnamon, clove, nutmeg (previously mixed with oil of lemon) with diluted alcohol. The tincture is mixed with fluidextract of senna (125 cc. to the liter) and then sucrose is dissolved in the mixture. *Dose.*—8 cc. (2 fluidrachms).

DOSES OF OFFICIAL SYRUPS

0.75 cc. (12 minims)	Syrup of ipecac (as an expectorant).
1 cc. (15 minims)	Syrup of ferrous iodide.
2 cc. (30 minims)	Syrups of squill and squill compound (N.F. VI).
4 cc. (1 fluidrachm)	Syrups of ammonium hypophosphite (N.F. VI), the bromides (N.F. VI), ephedrine sulfate (N.F. VI), hydriodic acid, ipecac and opium (N.F. VI), potassium guaiacolsulfonate (N.F. VI), senega (N.F. VI), white pine compound (N.F. VI), and white pine compound with morphine (N.F. VI).
8 cc. (2 fluidrachms)	Syrups of eriodictyon aromatic (N.F. VI), hypophosphites (N.F. VI), hypophosphites compound (N.F. VI), senna and trifolium compound (N.F. VI).
10 cc. (2½ fluidrachms)	Syrups of calcium lactophosphate (N.F. VI), ginger (N.F. VI), pine tar, rhubarb (N.F. VI), rhubarb aromatic, tolu balsam and wild cherry.
15 cc. (4 fluidrachms)	Syrups of ipecac (as an emetic) and sarsaparilla compound.

No dose is given the official syrups not named above, as they are used as bases for other medication or as adjuvants.

HONEYS

Honeys are *liquids containing medicines blended with honey.* In ancient times the honeys represented the most popular class of medicinal preparations, but in our present day of elixirs and of syrups the honeys are falling into disuse, although one is still recognized in the National Formulary. Honey itself is the natural product stored in the honeycombs by the bees, as explained on p. 706.

MEL—Honey

(Clarified Honey)

A saccharine secretion deposited in the honeycomb by the bee, *Apis mellifera* Linné (Fam. *Apidæ*). It must be free from foreign substances such as parts of insects, leaves, etc. but may contain pollen grains.

Summarized Description.

Thick syrupy, light yellow or yellowish-brown liquid, translucent when fresh; opaque and granular on standing, levorotatory; slightly acid to litmus paper. For details, see U.S.P., p. 229.

Possible Impurities.—Chlorides and sulfates, starch and dextrin, foreign coloring matter, azo dyes, artificial honey or added invert sugar. See U.S.P., p. 229.

Remarks.—In the recent revision, honey has been changed from a pharmaceutical preparation to a chemical substance. Up to the U.S.P. X, this ancient sweetening agent was called *Clarified Honey* (*mel depuratum*) and represented the natural product from the honeycomb clarified by directions given in the Pharmacopœia—mixing with shreds of wetted filter paper, heating on a water bath, removal of scum and filter paper as it rose to the surface of the heated liquid and final addition of 5 per cent of glycerin as a preservative. In the present Pharmacopœia, all mention of the process of clarification is omitted even in the rubric. The substance is considered as a chemical and chemical tests are provided to detect adulterants.

Mel Rosæ et Sodii Boratis or *Honey of Rose* and *Borax* (N.F.) is made by mixing glycerin (5 Gm.), borax (10 Gm.), and fluidextract of rose (10 cc.) with enough honey to make 100 Gm. This is a typical home remedy used particularly in treating canker sores in the mouth.

OXYMELS

Oxymels are liquid preparations in which the medicament is dissolved in or combined with a mixture of vinegar (or diluted acetic acid) and honey. They were important galenicals several centuries ago but at the present time there is practically only one survivor:

Oxymel Scillæ (N.F. V) is prepared by mixing 50 Gm. of vinegar of squill with 100 Gm. of honey and then heating the mixture on a water bath until it weighs 100 Gm.

BIBLIOGRAPHY

Solutions.—(General) Perrins, Ph. Jl., 120, 1928, 294 and 303. (Preservation) Berthelsen, Ph. Cent., 70, 1929, 37. (Donovan's solution) Donovan, Ph. Jl., 2, 1842, 469 and 546. (Lugol's solution) E. S., Jl. de ph., 15, 1829, 519; Lugol, Jl. de ph., 17, 1831, 381; Duhamel, A.J.P., 6, 1834, 115. (Compound solution of iodine) Parsons and Wittemore, Jl. Am. Ch. Soc., 33, 1911, 1933.

Isotonic Solutions.—Scoville, Jl. A.Ph.A., 12, 1923, 865; Knight, Ch. and Dr., 98, 1923, 59; Lehmann, Merck's Rept., 33, 1924, 13; Brown, Ph. Jl., 122, 1929, 324; *ibid.*, 132, 1934, 633; Gifford, Am. Dr., 94, July, 1936, 43.

Eye-drop Flask.—Driver, Ph. Zt., 55, 1910, 790.

Mucilages.—Schirmer, Arch. d. Pharm., 250, 1912, 230 and 241. (Mucilage of acacia) Sternberg, Ph. Weekbl., 65, 1928, 133.

Syrups.—(General) Dunn, A.Ph.A., 57, 1909, 950; Cook, A.Ph.A., 57, 1909, 1004. (Manufacture) Paddock, Dr. Circ., 24, 1880, 120; Bonvet, Am. Dr., 19, 1890, 129. (Stability) Forch, Sch. Wsch. Ch. Ph., 51, 1913, 136. Mayer, Jl. A.Ph.A., 4, 1915, 945; Kebler and Kunke, Jl. A.Ph.A., 13, 1924, 551. (Syrup as a solvent) Sturmer, Merck's Rept., 33, 1924, 10. (Syrup of acacia) Turner, Ph. Jl., 126, 1931, 160. (Easton's syrup) Anon., A.J.P., 39, 1867, 177. (Syrup of wild cherry) Umney, Nat. Dr., 40, 1910, 75; Kebler and Kunke, see above. (Senna syrups) Hommel, Merck's Rept., 18, 1909, 262. (Syrup of almond) Blondeau, A.J.P., 6, 1834, 353. (Syrup of tolu) Liverseege, Ph. Jl., 120, 1928, 93 and 141; Luck, Jl. A.Ph.A., 22, 1933, 844.

CHAPTER XIII

ELIXIRS, GLYCERITES, COLLODIONS, AND OLEATES

ELIXIRS

Elixirs are *hydro-alcoholic solutions of medicinal substances containing sucrose.* Therefore, it can be seen that there is a slight analogy between them and syrups. In the latter, however, there is much more sucrose. The National Formulary includes a so-called "aqueous elixir" which contains no alcohol. Considering the extensive use of elixirs, it may seem strange that so few have been introduced into the Pharmacopœia, but two (aromatic elixir, and elixir of glycyrrhiza) being included.

The chief reason for this is that the comparatively large doses of these pleasant alcoholic preparations cause fear that they are more to be regarded as tipples than as true medicinal agents. Therefore, the pharmacopœial committee omitted the long line of these elegant pharmaceuticals, leaving them for incorporation in the National Formulary, and a full list of the elixirs found in that book are tabulated on pages 228 to 230.

But another word concerning elixirs; do not fear that they will spoil. If properly made, they improve with age, for time enables the alcohol and aromatics to blend, making a smoother, more pleasant preparation.

Preparation.—The manufacture of most elixirs consists in the dissolving of the medicinal ingredients in aromatic elixir, elixir of glycyrrhiza, compound elixir of almond, N.F., elixir of anise, N.F. V, elixir aquosum, N.F., red aromatic elixir, N.F., elixir of bitter orange, N.F., compound elixir of cardamom, N.F., aromatic elixir of yerba santa, N.F. V, aqueous elixir of glycyrrhiza, N.F. V, compound elixir of taraxacum, N.F., iso-alcoholic elixir, N.F., compound elixir of vanillin, N.F., or some other pleasantly flavored basic elixir. Among the latter we find compound elixir of pepsin, N.F., Scoville's *aromatic chocolate elixir* containing chocolate, compound tincture of vanillin, coumarin, and oils of orange, peppermint, anise, coriander, caraway, and Ceylon cinnamon and the Snow-Fantus *aromatic elixir of saccharin,* a pleasantly flavored sugar-free elixir for use by diabetics.

Elixirs should be clear when dispensed. The flavoring substances, used in elixirs, mainly volatile oils, must be fresh and of the finest quality if satisfactory products are desired. On mixing the ingredients of elixirs, a cloudy liquid usually results. This will not filter clear immediately through paper. After standing several hours a clear liquid is more readily obtained upon filtration. The addition of 10 or 20 Gm. of purified talc to the liquid, shaking and allowing the liquid to stand and subsequent filtration usually produces a clear product. Excessive amounts of filtering media and colloidal clays or media containing free alkali or carbonates must be avoided. Direct sunlight and extreme temperatures tend to decompose elixirs. They should be preserved in tightly stoppered bottles at room temperature.

ELIXIR AROMATICUM—Aromatic Elixir

(Elix. Arom.—Simple Elixir)

Condensed Recipe.

Ingredients.—Compound spirit of orange, 12 cc.; syrup, 375 cc.; alcohol; distilled water enough to make 1 liter. Purified talc, as clarifier.

Manipulation.—The spirit is dissolved in 238 cc. of alcohol; the syrup is added followed by enough distilled water to measure 1000 cc. To this fluid the talc is added and the mixture is filtered through a wetted filter. For details, see U.S.P., p. 137.

Remarks.—This is a pleasantly flavored preparation, provided the compound spirit of orange (p. 203) is made from fine oils. It is the basis of most elixirs, among them the official *elixir of glycyrrhiza.*

Shiflett and also Silver object to the U.S.P. method of manufacture of this elixir, preferring to save time by adding the syrup to the filtered hydro-alcoholic solution. Krantz prefers to use magnesium carbonate as the filtering agent.

ELIXIR GLYCYRRHIZÆ—Elixir of Glycyrrhiza (Elix. Glycyrrh.—Elixir Adjuvans—Elixir of Licorice)

Condensed Recipe.

Fluidextract of glycyrrhiza (125 cc.) is mixed with enough aromatic elixir to make 1 liter. For details, see U.S.P., p. 138.

Remarks.—This preparation was recognized in U.S.P. VIII under the name, *elixir adjuvans.* It originally appeared in the National Formulary and the name just given indicates that it is intended as a pleasant addition to mixtures of bitter drugs, the glycyrrhiza being an admirable mask for bitter substances. No dose is given by the Pharmacopœia.

Elixir Iso-Alcoholicum (N.F. VI) also known as *Iso-Elixir* is intended to supply a vehicle of varying alcoholic strength to suit the needs of drugs or combinations of drugs having different solubilities in alcohol or hydro-alcoholic solvents. The general directions are to mix a certain volume of low-alcoholic elixir with a certain volume of high-alcoholic elixir. The *low-alcoholic elixir* containing 8 to 10 per cent by volume of alcohol is made by mixing alcohol, glycerin, and distilled water, adding compound spirit of orange, agitating thoroughly from time to time and allowing it to stand twenty-four hours, filtering through hard paper until clear and dissolving sucrose in the filtrate by agitation or percolation. The *high-alcoholic elixir,* containing 73 to 78 per cent alcohol by volume, is made by dissolving compound spirit of orange and saccharin in alcohol, adding glycerin, mixing and filtering. By proper blending of the low- and high-alcoholic elixirs an elixir of almost any desired alcoholic content can be obtained. A table for adjustment of iso-alcoholic elixir is given on page 118 of N.F. VI covering vehicles from 10 to 95 per cent alcohol. For liquid galenicals employ an elixir of an alcoholic strength equivalent to the menstruum employed. For galenicals of different alcoholic strengths in the same prescription employ an elixir of the average alcoholic strength of the several ingredients. It is advisable always to use the lowest alcoholic strength that will yield a clear solution.

Elixir Ferri, Quininæ et Strychninæ Phosphatum (U.S.P. VIII; N.F. VI) is prepared from soluble ferric phosphate, quinine phosphate, strychnine phosphate (0.250 Gm. per liter), alcohol, glycerin, oil of orange and distilled water. It should not be dispensed if markedly darkened in color. This preparation is an improvement over the U.S.P. VIII product which was made from soluble ferric phosphate, quinine, strychnine (0.275 Gm. to the liter), with the aid of phosphoric acid and of a solution of ammonium acetate (prepared from ammonium carbonate and acetic acid). The vehicle was aromatic elixir and much care had to be exercised in order to secure a handsome product. Its keeping qualities were far from good, so it was decided to drop the preparation both from the Pharmacopœia and from the National Formulary V. Burt claims that the decomposition of this elixir is due to the action of ferric ion upon the citric acid, which is broken into acetone, carbon dioxide, and water.

Elixir Calcii Lactophosphatis (N.F. VI) is made by dissolving precipitated calcium carbonate in lactic and phosphoric acids and adding to the solution of lactophosphate thus formed, syrup, compound spirit of orange, alcohol and distilled water. *Dose.*—8 cc. (2 fluidrachms).

Elixir Cinchonæ Alkaloidorum (N.F. VI) is a preparation rather poorly replacing the original elixir of calisaya, which was made by percolating calisaya bark and aromatics with a hydro-alcoholic menstruum, detannating the resulting tincture with fresh ferric hydroxide and adding to the detannated preparation, sugar, flavor and color. The Formulary product is made by dissolving the sulfates of quinine, cinchonine and cinchonidine in aromatic elixir; compound tincture of cudbear being used as color. Each liter contains 2 Gm. of the quinine and 1 Gm. each of the cinchonine and cinchonidine sulfates.

Elixir Pepsini Compositum (N.F. VI) is a modified form of the *compound digestive elixir* of the earlier Formularies. Introduced as a dyspepsia remedy under various trade names such as *elixir of lactated pepsin,* etc., and containing pepsin, pancreatin and diastase, it was violently attacked by exponents of modern therapy on the ground that it was a therapeutic monstrosity (p. 955). Its wide vogue as a vehicle caused the National Formulary revision committee to readmit it with the pancreatin and diastase omitted.

THE ELIXIRS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Elixir aminopyrinæ.	Elixir of aminopyrine.	Aminopyrine, 40 Gm.; compound spirit of orange; alcohol; glycerin; syrup; distilled water. Compound tincture of cudbear as color.	*Dose.*—4 cc. (1 fluidrachm).
Elixir ammonii bromidi.	Elixir of ammonium bromide.	Ammonium bromide, 85 Gm.; syrup; distilled water; aromatic elixir.	*Dose.*—4 cc. (1 fluidrachm).
Elixir ammonii valeratis.	Elixir of ammonium valerate.	Acid ammonium valerate, 35 Gm.; chloroform, 2 cc.; tincture of vanilla; aromatic elixir. Ammonia water enough to dissolve the valerate and compound tincture of cudbear as color.	*Dose.*—4 cc. (1 fluidrachm).
Elixir amygdalæ compositum.	Compound elixir of almond.	Oil of bitter almond; vanillin; orange flower water; alcohol, 50 cc.; syrup; distilled water.	This and the three which follow are pleasantly flavored basic elixirs, which provide an admirable variety of flavors for the extemporaneous preparation of medicinal elixirs.
Elixir aquosum.	Aqueous elixir.	Vanillin; oils of bitter almond and fennel; chloroform; glycerin; orange flower water; syrup; purified talc; distilled water.	
Elixir aromaticum rubrum.	Red aromatic elixir.	Aromatic elixir, U.S.P., colored with tincture of cudbear.	
Elixir aurantii amari.	(Replacing elixir curassao N.F. III.)	Oil of bitter orange; tincture of bitter orange peel; alcohol, 300 cc.; orange flower water; syrup; distilled water.	
Elixir barbitali.	Elixir of barbital.	Barbital, 35 Gm.; caramel; compound spirit of vanillin; alcohol; glycerin.	*Dose.*—4 cc. (1 fluidrachm).
Elixir bismuthi.	Elixir of bismuth.	Glycerite of bismuth; glycerin; distilled water; aromatic elixir.	*Dose.*—4 cc. (1 fluidrachm).
Elixir bromidorum quinque.	Elixir of five bromides.	Sodium bromide, 87 Gm.; potassium bromide, 70 Gm.; calcium bromide, 52 Gm.; lithium bromide, 35 Gm.; ammonium bromide, 17 Gm.; syrups of glycyrrhiza and raspberry; aromatic elixir; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir bromidorum trium.	Elixir of three bromides.	Bromides of ammonium, potassium and sodium, of each 80 Gm.; compound elixir of almond; solution of amaranth as color.	*Dose.*—4 cc. (1 fluidrachm).
Elixir buchu.	Elixir of buchu.	Buchu; alcohol; compound spirit of orange; sucrose; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir buchu compositum.	Compound elixir of buchu.	Compound fluidextract of buchu; aromatic elixir.	*Dose.*—4 cc. (1 fluidrachm).
Elixir buchu et potassii acetatis.	Elixir of buchu and potassium acetate.	Potassium acetate, 85 Gm.; elixir of buchu.	*Dose.*—4 cc. (1 fluidrachm)
Elixir buchu, juniperi et potassii acetatis.	Elixir of buchu, juniper and potassium acetate.	Buchu; juniper; potassium acetate, 50 Gm.; alcohol; sucrose; compound spirit of orange; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir calcii et sodii glycerophosphatum.	Elixir of calcium and sodii glycerophosphates.	Glycerophosphates of calcium and sodium; phosphoric acid; glycerin; aromatic elixir; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir calcii lactophosphatis.	Elixir of calcium lactophosphate.	....	See p. 227.
Elixir cardamomi compositum.	Compound elixir of cardamom.	Compound spirit of cardamom, 10 cc.; alcohol, 90 cc.; syrup; distilled water.	

THE ELIXIRS OF THE NATIONAL FORMULARY—(*Continued*)

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Elixir carnis et ferri.	Elixir of beef and iron.	Extract of beef, 35 Gm.; iron and ammonium citrate; alcohol, 200 cc.; compound spirit of orange; syrup; distilled water.	Replacing *beef, wine and iron* (N.F. IV) *Dose.*—8 cc. (2 fluidrachms).
Elixir cascaræ sagradæ.	(Elixir rhamni purshianæ N.F. III.)	Aromatic fluidextract of cascara sagrada, 500 cc.; syrup of glycyrrhiza.	*Dose.*—4 cc. (1 fluidrachm).
Elixir catariæ et fœniculi.	Elixir of catnep and fennel.	Catnep; sodium bicarbonate; fennel; spearmint; alcohol; sucrose; distilled water.	*Dose* (for infants) 0.5 cc. (8 minims).
Elixir chloralis et potassii bromidi compositum.	Compound elixir of chloral and potassium bromide.	Chloral hydrate; potassium bromide; extracts of cannabis and hyoscyamus; sucrose; caramel; pumice; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir cinchonæ alkaloidorum.	Elixir of calisaya alkaloidal.	....	See p. 227.
Elixir euphorbiæ compositum.	Antiasthmatic elixir.	Fluidextracts of euphorbia pilulifera and lobelia; sodium bromide, 35 Gm.; sodium iodide, 35 Gm.; spirit of nitroglycerin; compound tincture of cardamom; oil of peppermint; glycerin; alcohol, 200 cc.; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir ferri quininæ et strychninæ.	Elixir of iron, quinine and strychnine.	Tincture of ferric citrochloride; quinine hydrochloride; strychnine sulfate, 0.175 Gm.; alcohol; glycerin; distilled water. Compound spirit of orange as flavor.	This is *not* the elixir of the phosphates of iron, quinine and strychnine. See p. 227. *Dose.*—4 cc. (1 fluidrachm).
Elixir ferri, quininæ et strychninæ phosphatum.	Elixir of iron, quinine and strychnine phosphates.	Soluble ferric phosphate; quinine phosphate; strychnine phosphate; oil of orange; alcohol; glycerin; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir gentianæ.	Elixir of gentian.	Fluidextract of gentian; sodium citrate; glycerin; syrup; alcohol; distilled water. Compound spirit of cardamom as flavor.	
Elixir gentianæ et ferri.	Elixir of gentian and iron.	Tincture of ferric citrochloride, 100 cc.; elixir of gentian.	*Dose.*—4 cc. (1 fluidrachm).
Elixir gentianæ glycerinatum.	Glycerinated elixir of gentian.	Fluidextracts of gentian and taraxacum; tinctures of sweet orange peel and cardamom, compound; syrup of raspberry; ethyl acetate; phosphoric acid; glycerin, sucrose alcohol, 100 cc.; distilled water.	See p. 716. *Dose.*—8 cc. (2 fluidrachms).
Elixir glycerophosphatum compositum.	Compound elixir of glycerophosphates.	Glycerophosphates of sodium, calcium, iron and manganese; quinine hydrochloride; strychnine nitrate; lactic acid; citric acid; compound spirit of cardamom; alcohol; glycerin; distilled water.	*Dose.*—8 cc. (2 fluidrachms).
Elixir guaranæ et apii.	Elixir of guarana and celery.	Fluidextracts of guarana, celery fruit and glycyrrhiza; glycerin; aromatic elixir.	*Dose.*—8 cc. (2 fluidrachms).
Elixir hydrangeæ et lithii.	Elixir of hydrangea and lithium	Hydrangea is percolated with alcohol, glycerin and water flavored with compound spirit of orange. In the percolate are dissolved lithium benzoate and salicylate, of each 26 Gm.; and sucrose.	*Dose.*—4 cc. (1 fluidrachm).
Elixir hydrastis compositum.	Alkaline elixir.	Fluidextracts of hydrastis, avena sativa, xanthoxylum, gentian and ginger; sodium bicarbonate, 8 Gm.; aromatic elixir.	*Dose.*—4 cc. (1 fluidrachm).
Elixir iso-alcoholicum.	Iso-alcoholic elixir.	Low-alcoholic elixir; high-alcoholic elixir.	See p. 227.

THE ELIXIRS OF THE NATIONAL FORMULARY—(*Continued*)

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Elixir pepsini.	Elixir of pepsin.	Pepsin, 35 Gm.; citric acid; exsiccated sodium phosphate; distilled water; glycerin; aromatic elixir.	*Dose.*—8 cc. (2 fluiddrachms).
Elixir pepsini, bismuthi et strychninæ.	Elixir of pepsin, bismuth and strychnine.	Strychnine, 125 mg. tartaric acid; elixir of pepsin and bismuth.	*Dose.*—8 cc. (2 fluidrachms).
Elixir pepsini compositum.	Compound digestive elixir.	Pepsin, 35 Gm.; lactic acid; glycerin; alcohol, 200 cc.; oil of orange; distilled water. Cudbear as color.	*Dose.*—8 cc. (2 fluidrachms). See p. 227.
Elixir pepsini et bismuthi.	Elixir of pepsin and bismuth.	Pepsin, 18 Gm.; glycerite of bismuth, 125 cc.; glycerin, distilled water; caramel; aromatic elixir.	*Dose.*—8 cc. (2 fluidrachms).
Elixir pepsini et rennini.	Essence of pepsin.	Pepsin, 45 Gm.; rennin, 18 Gm.; tincture of sweet orange peel; glycerin; alcohol, 165 cc.; oil of myristica; distilled water.	*Dose.*—8 cc. (2 fluidrachms).
Elixir phenobarbitali.	Elixir of phenobarbital.	Phenobarbital, 4 Gm.; tinctures of sweet orange peel and cudbear; alcohol; glycerin; syrup; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir phosphori	Elixir of phosphorus.	Phosphorus, 150 mg.; chloroform, 5 cc.; alcohol, 340 cc.; glycerin; compound spirit of orange; oil of anise; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir potassii bromidi.	Elixir of potassium bromide.	Potassium bromide, 175 Gm.; syrup; distilled water, aromatic elixir.	*Dose.*—4 cc. (1 fluidrachm).
Elixir rhei alkalinum.	Alkaline elixir of rhubarb.	Fluidextracts of rhubarb and hydrastis; potassium carbonate; tincture of cinnamon; spirit of peppermint, syrup; diluted alcohol.	Mistura rhei alkalina (N F. V.). *Dose.*—4 cc. (1 fluidrachm).
Elixir sabal et santali compositum.	Compound elixir of sabal and sandalwood.	Fluidextracts of zea and sandalwood; compound spirit of orange; glycerin, oil of santal; alcohol; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir sodii bromidi.	Elixir of sodium bromide.	Sodium bromide, 175 Gm.; syrup; distilled water; aromatic elixir.	*Dose.*—4 cc. (1 fluidrachm).
Elixir sodii salicylatis.	Elixir of sodium salicylate.	Sodium salicylate, 85 Gm.; syrup; distilled water; aromatic elixir.	*Dose.*—4 cc. (1 fluidrachm).
Elixir sodii salicylatis compositum.	Compound elixir of sodium salicylate.	Sodium salicylate; fluidextracts of cimicifuga and gelsemium; potassium iodide; aromatic elixir.	*Dose.*—4 cc. (1 fluidrachm).
Elixir sodii thiocyanatis.	Elixir of sodium sulfocyanate.	Sodium thiocyanate, 40 Gm.; sodium phosphate; soluble saccharin; alcohol; syrups of orange, eriodictyon aromatic and sarsaparilla compound; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir taraxaci compositum.	Compound elixir of taraxacum.	Fluidextracts of taraxacum, wild cherry and glycyrrhiza; tinctures of sweet orange peel, cinnamon and cardamom compound; glycerin; aromatic elixir.	
Elixir terpini hydratis.	Elixir of terpin hydrate.	Terpin hydrate, 17 Gm.; tincture of sweet orange peel; spirit of bitter almond; alcohol, 425 cc.; glycerin; syrup; distilled water.	*Dose.*—4 cc. (1 fluidrachm).
Elixir terpini hydratis et codeinæ.	Elixir of terpin hydrate and codeine.	Codeine, 2 Gm.; elixir of terpin hydrate.	*Dose.*—4 cc. (1 fluidrachm).
Elixir vanillini compositum.	Compound elixir of vanillin.	Compound spirit of vanillin, 20 cc.; alcohol, 80 cc.; glycerin; syrup; distilled water. Caramel as color.	
Elixir viburni opuli compositum.	Compound elixir of cramp bark.	Fluidextracts of viburnum opulus, trillium and aletris; compound elixir of taraxacum, glycerin.	*Dose.*—4 cc. (1 fluidrachm).
Elixir viburni prunifolii.	Elixir of black haw.	Fluidextract of viburnum prunifolium; compound tincture of cardamom; aromatic elixir, glycerin.	*Dose.*—4 cc. (1 fluidrachm).

Vehiculæ is the name suggested by L. Emanuel for class of preparations intended to serve as pleasant vehicles for medicinal substances and not having the objections possessed by elixirs; the fact that they are strongly alcoholic.

Fantus and his coworkers have conducted extensive investigations on the preparation of palatable vehicles for medicaments. In addition to the elixirs described on page 228, Dr. Fantus favors syrup of cinnamon for salicylates, a flavored syrup of acacia for urea and syrup of raspberry and syrup of cherry for a number of medicinal chemicals.

Eschenbrenner suggests disguising the taste of medicines, with the use of yerba santa for quinine, trisodium phosphate for veronal and acid sodium phosphate for morphine.

GLYCERITES

Glycerites (or *glycerols*) are *mixtures* or *solutions of medicinal substances with glycerin.* Most of them are solutions, but one of those official (glycerite of starch) is a semisolid mass. The glycerites are excellent preparations, being both permanent and emollient. However, they have the disadvantage of being smeary like their basic solvent.

TABLE OF OFFICIAL GLYCERITES

Process	*Galenic Preparations*	*Chemical Preparations*
Cold solution.	Glycerite of egg yolk (N.F. VI).	
	Glycerite of iodine and zinc iodide (N.F. VI).	
	Glycerite of pepsin (N.F. VI).	
	Glycerite of phenol (N.F. VI).	
	Glycerite of tragacanth (N.F. VI).	
Warm solution.	Glycerite of tannic acid.	Glycerite of boroglycerin.
	Glycerite of starch.	Glycerite of bismuth (N.F. VI).

SPECIAL NOTES ON OFFICIAL GLYCERITES

GLYCERITUM ACIDI TANNICI—Glycerite of Tannic Acid

(Glycer. Acid. Tan.—Glycerite of Tannin)

Condensed Recipe.

Tannic acid (20 Gm.) and sodium citrate (1 Gm.) are dissolved in glycerin (79 Gm.) by rubbing in a porcelain dish and heating to 115° to 120° C. on a sand bath until dissolved. For details, see U.S.P., p. 180.

Remarks.—Glycerite of tannic acid is a 20 per cent solution of tannic acid in glycerin containing 1 per cent of sodium citrate as a preservative. It is hardly necessary to say that the use of metallic utensils should be rigidly avoided, as tannin combines with metals, particularly with iron, forming with that metal an inky black compound.

The glycerite when first prepared is of a brownish color, but on standing it assumes a deep green tint.

It is a convenient form for dispensing solutions of tannic acid, it being readily diluted by the addition of as much water as necessary.

GLYCERITUM AMYLI—Glycerite of Starch

(Glycer. Amyl.)

Condensed Recipe.

Ingredients.—Starch, 10 Gm.; distilled water, 20 cc.; glycerin, 70 cc.

Manipulation.—The starch is triturated with the distilled water, is added to the glycerin, warmed to 140° C. and the mixture is heated between 140° and 144° C. until a jelly forms. For details, see U.S.P., p. 181.

Remarks.—Glycerite of starch is a jelly containing 10 per cent of starch, made by blending starch, water, and glycerin, and gently warming, with constant stirring, on a sand bath to 144° C. to insure rupture of the starch granules. (See p. 705.) The stirring is necessary to avoid scorching.

Glycerite of starch is used as a basis of enemas and also as a pill excipient. Not being used internally, no dose is given by the Pharmacopœia.

GLYCERITUM BOROGLYCERINI—Glycerite of Boroglycerin

(Glycer. Boroglyc.)

Storage.—Preserve in well-closed containers.

Condensed Recipe.

Ingredients.—Boric acid, 310 Gm.; glycerin, enough to make 1000 Gm.

Manipulation.—The boric acid is added to 460 Gm. glycerin that has been heated to 150° C. and the mixture is heated until it weighs 500 Gm. Mix this with 500 Gm. glycerin. For details, see U.S.P., p. 181.

Remarks.—Glycerite of boroglycerin contains 50 per cent of boroglycerin (for calculations, see p. 681), and is a thick, viscid liquid, which is used externally as an antiseptic and emollient dressing. It is well to bear in mind that the addition of water to this glycerite causes precipitation of boric acid and that in making any dilution of this glycerite stronger than 1 part of acid to 18 parts of fluid, glycerin should be employed.

Glyceritum Phenolis (U.S.P. X; N.F. VI) or *Glycerite of Phenol,* also known as *Glycerite of Carbolic Acid* is prepared by dissolving 20 cc. of liquefied phenol in 79 cc. of glycerin and adding sodium citrate, dissolved in distilled water.

It is a 20 per cent solution of liquefied phenol in glycerin and is an admirable antiseptic. For ordinary use, however, it is too concentrated and more advantageous is the so-called *carbolated glycerin,* containing 1 fluidrachm of phenol to the fluidounce of the finished product. *Dose.*—0.3 mils (5 minims).

DOSES OF GLYCERITES

0.3 cc. (5 minims)	Glycerite of phenol (N.F. VI)
2 cc. (30 minims)	Glycerite of pepsin (N.F. VI)

No dose given of glycerite of boroglycerin, glycerite of starch, glycerite of tannic acid, glycerite of bismuth (N.F. VI), glycerite of iodine and zinc iodide (N.F. VI), glycerite of egg yolk (N.F. VI), and glycerite of tragacanth (N.F. VI).

Glyceritum Hydrastis (U.S.P. IX) or *Glycerite of Hydrastis* is practically a glycerinic fluidextract of that important drug. It is prepared by percolating the drug with alcohol, evaporating off the alcohol, and blending the filtered residue with glycerin. It represents a form of "fluid hydrastis" so largely used as an ingredient of gonorrheal injections.

Glyceritum Bismuthi (N.F.) is a preparation representing about 13 Gm. bismuth oxide in 100 cc. made by treating a solution of bismuth subnitrate in a diluted nitric acid with water and then mixing with tartaric acid and sodium bicarbonate. The magma so obtained is washed after which it is heated with more tartaric acid and sodium bicarbonate until the resulting bismuth sodium tartrate has dissolved. To this solution glycerin and water are added.

Glyceritum Ovi Vitelli (N.F.) or *Glyconin* is made by rubbing 45 Gm. of yolk of egg with 55 Gm. of glycerin. A thick yellow mixture results, which affords one of the most striking illustrations of the antiseptic action of glycerin. The writer has known a sample of glycerite of the yolk of egg five years old to be as sweet as when first made.

Glycerite of Elm has been suggested by Hommel as a vehicle for iodides and for creosote; while

Glycerite of Iodine containing 20 parts of iodine, 20 parts of potassium iodide, and 20 parts of glycerin is recommended by Apple.

GLYCERITES OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 mils).	Remarks.
Glyceritum bismuthi.	Glycerite of bismuth.	....	See p. 232.
Glyceritum iodi et zinci iodidi.	Glycerite of iodine and zinc iodide.	Zinc iodide; iodine; glycerin; distilled water.	Diluted Talbot's solution. Keep in glass or rubber stoppered bottles.
Glyceritum ovi vitelli.	Glycerite of yolk of egg.	....	See p. 232.
Glyceritum pepsini.	Glycerite of pepsin.	Pepsin, 100 Gm.; diluted hydrochloric acid; glycerin; distilled water.	*Dose.*—2 cc. (30 minims).
Glyceritum phenolis.	Glycerite of phenol.	Liquefied phenol, sodium citrate; distilled water; glycerin.	*Dose.*—0.3 cc. (5 minims).
Glyceritum tragacanthæ	Glycerite of tragacanth	Tragacanth; glycerin; water.	See p. 331.

COLLODIONS

These are *preparations used externally, having as their base collodion,* which liquid is a solution of pyroxylin (gun cotton) in alcohol and ether (p. 703).

The solvent readily evaporates, leaving a film of gun cotton, which is an excellent protective.

TABLE OF OFFICIAL COLLODIONS
(All Galenic)

Made by simple solution	Collodion. Compound salicylic collodion (N.F. VI). Flexible collodion. Styptic collodion (N.F. VI).
Made by percolation and solution	Cantharidal collodion (U.S.P. IX).

SPECIAL NOTES ON OFFICIAL COLLODIONS

COLLODIUM—Collodion
(Collod.)

Storage.—Preserve in well-closed containers, in a cool place, remote from fire.

Condensed Recipe.

Mix 40 Gm. pyroxylin with 250 cc. alcohol and 750 cc. ethyl oxide. Shake until the pyroxlin is dissolved and decant clear fluid. For details, see U.S.P., p. 129.

Description.—Clear or slightly opalescent syrupy liquid; inflammable; evaporated in thin layer, leaves a film of pyroxylin. For details, see U.S.P., p. 129.

Assay.—Precipitate out the pyroxylin by addition of an equal volume of water. Pyroxylin obtained should represent 5.1 per cent of the collodion taken. For details, see U.S.P.

Remarks.—This ethereal solution of gun cotton will be discussed later (p. 703).

COLLODIUM FLEXILE—Flexible Collodion
(Collod. Flex.)

Storage.—Preserve in well-closed containers, in a cool place, remote from fire.

Condensed Recipe.

Mix 950 Gm. collodion, 20 Gm. camphor and 30 Gm. castor oil and shake until the camphor is dissolved. For details, see U.S.P., p. 130.

Remarks.—The pure pyroxylin layer left on evaporation of ordinary collodion is brittle and apt to crack when placed on the knuckles and other joints. Flexible collodion, on the other hand, is made pliable by the addition of camphor and castor oil.

Note that as collodion is a solution of gun cotton in a mixture of alcohol and ether, it will be precipitated by the addition of water. Therefore, a prescription containing collodion, tincture of iodine, and water of ammonia cannot be compounded, for as soon as the water of ammonia is added to the collodion, the pyroxylin separates in a wad. This can be remedied by substitution of the spirit of ammonia for water of ammonia.

All the collodions, since they contain ether, must be handled carefully and kept away from the flame.

Collodium Cantharidatum (U.S.P. IX) or *Cantharidal Collodion* is prepared by percolating cantharides with acetone, distilling the solvent from the percolate, and dissolving the remaining extract in flexible collodion. The Swiss Pharmacopœia directs that this collodion be made from cantharidin.

COLLODIONS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 100 cc.).	Remarks.
Collodium salicylicum compositum	Compound salicyclic collodion.	Salicylic acid, 10 Gm ; fluidextract of cannabis, 10 cc.; flexible collodion.	The well-known "corn solvent." See p. 859.
Collodium stypticum.	Styptic collodion.	Tannic acid, 16 Gm ; flexible collodion.	Was listed in U.S.P. VIII.

OLEATES

These are *solutions of metallic oxides or alkaloids in oleic acid*, and, like ointments, produce the physiologic effect of the active ingredient through absorption of the latter on application to the skin by inunction.

They are prepared by dissolving an oxide or an alkaloid in oleic acid, and in making metallic oleates an excess of heat should be avoided, as oleic acid easily reduces the metallic oxides to the metals, particularly when the mixture is heated. The dissolving of the oxides in oleic acid is sometimes a rather difficult matter, and in order to obtain good results the oxide should be *in a very fine* powder and should be triturated with alcohol or shaken with ether prior to adding the oleic acid. The volatile fluid is, of course, evaporated after the oxide has dissolved. In making an oleate of an alkaloid, the free alkaloid and not the salts thereof should be used. All the oleates are, strictly speaking, chemical preparations, since the solvent (oleic acid) forms a salt (oleate) with either a metallic oxide or an alkaloid. Bear in mind, however, that the pharmaceutical oleates, now considered, are not definite chemicals, like sodium oleate (soap), lead oleate (lead plaster), or the other oleates discussed in Chapter XLI. The class we are now considering contains a large amount of oleic acids and, therefore, represents the definite chemical (the true oleate) dissolved in an excess of oleic acid.

OLEATUM HYDRARGYRI—Oleate of Mercury
(Oleat. Hydrarg.)

Oleate of Mercury is a solution of mercuric oleate in oleic acid corresponding to not less than 24 per cent and not more than 26 per cent of HgO.

Storage.—Preserve in tightly-closed containers, protected from strong light, and do not dispense it if globules of mercury are separated at the bottom of the container.

Condensed Recipe.

Ingredients.—Yellow mercuric oxide, 25 Gm.; oleic acid, enough to make 100 Gm.

Manipulation.—Mix the oxide with the oleic acid, warm the mixture to 50° C. with stirring until the oxide has dissolved. For details, see U.S.P., p. 245.

Description.—Yellowish-brown ointment-like mass, slightly soluble in alcohol, ether, and fixed oils. For details, see U.S.P., p. 245.

Assay.—See U.S.P., p. 245.

Remarks.—This is the only oleate recognized in the present Pharmacopœia. In making it, it is best to triturate the oxide with alcohol prior to adding the oleic acid. It is used for extinguishing the mercury in the manufacture of mercurial ointment. In its manufacture, all contact with metallic utensils should be avoided.

There are no oleates listed in the N.F. VI. The N.F. V listed oleate of quinine used to obtain physiological effects of that alkaloid by inunction and oleate of veratrine.

BIBLIOGRAPHY

Elixirs.—(History) "X-rayser II," Ch. & Dr., 93, 1920, 1699. (General), Edel, A.J.P., 43, 1871, 322. Fantus, Jl. A.Ph.A., 9, 1920, 708; Fantus and Snow Jl. A.Ph.A., 10, 1921, 277. (Basic elixirs) Beringer, Pharm. Era, 42, 1910, 622. (Aromatic elixir) Hancock and others, A.J.P., 46, 1874, 83; Shiflett, Pract. Dr. 47, Mch., 1930, 17; Silver, *ibid.*, 47, Apr., 1930, 37; Krantz and Carr, Jl. A.Ph.A., 19, 1930, 1095; (Elixir of calisaya) Diehl, A.J.P., 40, 1867, 105. (Essence of pepsin) Wetterstroem Dr. Circ., 54, 1910, 457. (Elixir of phosphate of iron, quinine and strychnine) Marquier, Apothecary, 7, 1910, 20; Burt, Jl. A.Ph.A., 17, 1928, 650. (Elixir of ammonium valerate) Enos, A.J.P., 33, 1861, 345. (Elixir of terpin hydrate) Webb, Bull. A.Ph.A., 1910, 421. (Aromatic chocolate elixir) Scoville, Bull. Pharm., 24, 1910, 174. (Aromatic elixir of saccharin) Snow and Fantus, Jl. A.Ph.A., 19, 1930, 1007.

Vehicles.—Emanuel, A.Ph.A., 58, 1910, 71; Fantus and co-workers, Jl. A.Ph.A., 22, 1933, 323 & 757; *ibid.*, 23, 1934, 127, 232, 698, 812 & 915.

Taste Disguisers.—Eschenbrenner, Ph. Zt., 74, 1929, 93.

Glycerites.—(Boroglycerin) McElhenie, Dr. Circ., 26, 1882, 97. (Starch) Alcock, Ch. & Dr., 84, 1914, 478. (Elm) Hommel, Merck's Rep., 18, 1909, 234. (Iodine) Apple, Merck's Rep., 18, 1909, 300.

Collodion.—(Manufacture) Parrish, A.J.P., 21, 1849, 289; Caspari, A.Ph.A., 7, 1858, 6; Maynard, A.Ph.A., 15, 1867, 164. (Cantharidal) "E. B.," Sch. Wsch. Ch. Ph., 50, 1912, 673.

Oleates.—(History and description) Shoemaker, The Oleates, 1885. (Manufacture) Beringer, A.Ph.A., 59, 1911, 783. (Mercury) Dieterich, Merck's Rep., 18, 1909, 269; Dyer and Metcalfe, Pharm. J., 115, 1925, 145 and 180.

CHAPTER XIV

INFUSIONS, DECOCTIONS, AND TINCTURES

INFUSIONS

Infusions are *preparations made by the maceration or percolation of vegetable substances with water*. At times dilute alcohol is used in a portion of the extraction operation or alcohol may be added as a partial preservative. With infusions we begin the study of those preparations made by extraction—by use of the processes of maceration and percolation—rather than by the simple solution of the medicating substance with the diluent.

In some infusions the water used as the extracting solvent is applied cold, but usually it is poured on while boiling hot. It is used cold for such drugs as wild cherry, the active principle of which, hydrocyanic acid, would be driven off or the formation of which would be prevented by the temperature of boiling water.

Infusions are not much used in this country, American physicians preferring the alcoholic preparations of drugs, such as tinctures and fluidextracts. They have been eliminated entirely from the U.S.P.

They quickly spoil, and should be freshly prepared whenever called for, which is one reason why they have lost their popularity in this country. They are still largely used in England, and the various infusion mugs depicted in works of pharmacy are mostly of English design. Note that while no infusions are official in the U.S.P., a general formula is given by which all unofficial infusions save those of potent drugs are to be prepared.

TABLE OF OFFICIAL INFUSIONS

Manufacture	*Preparations*
Maceration with hot water.	Infusion of digitalis (N.F. VI). Infusion of senna, with magnesium sulfate (U.S.P. IX; N.F. VI).
Percolation with dilute alcohol and adding cold water.	Compound infusion of gentian (N.F. VI).

Explanatory of the table given above, it may be said that in making infusions by *hot maceration* the coarsely ground drug is put into a suitable vessel, boiling water is poured upon it, and the maceration permitted to continue a half hour or an hour.

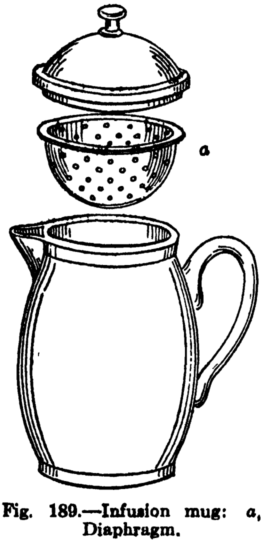


Fig. 189.—Infusion mug: *a*, Diaphragm.

In England, where a dozen different infusions may be called for in a day's prescription business, those infusions in daily demand are prepared freshly each morning, and the special infusion mugs, such as are shown in Fig. 189, are in general use. In this country, where a prescription for an infusion comes in but rarely, any suitable glass or porcelain vessel—say, a teapot or a beaker—can be used. It is convenient to prepare the infusion by circulatory solution, that is, the ground drug is placed in a small piece of straining cloth and suspended just below the surface of the boiling water. It might be stated that the perforated diaphragm *a* of the infusion mug pictured above is intended for the same purpose. The process of *cold maceration* is sometimes employed in making infusions, but this is done rarely, and is not given official sanction. The process is identical with hot maceration, save that cold water is used. The process of *cold percolation* is directed for such drugs as wild cherry.

The process of *hot percolation* is sometimes employed in making infusions, but is not given official sanction. It might, however, be mentioned that the first stage in the manufacture of the official fluidextracts of cascara sagrada (p. 268) and of glycyrrhiza (p. 269) is the preparation of an infusion by percolation with hot water.

Infusions are sometimes prepared by *digestion*, that is, by allowing the drug to macerate in water several hours at gentle heat, such as that furnished by a steam radiator or found at the back of a wood-stove or coal range.

But one word is necessary as to the preparation of infusions by diluting fluidextracts with warm water, a process recommended, for scarcely disinterested reasons, on the labels of the fluidextracts of most manufacturers.

That necessary word is *don't!* The only reason an American physician prescribes an infusion is to get only those active principles of a drug which are soluble in water. If he wants those principles which are soluble in alcohol, he prescribes a tincture or a fluidextract. Hence for the pharmacist to dispense an infusion made from a fluidextract is as much a perversion of duty as would be the dispensing of a watery percolate from ginger on a prescription calling for the official tincture.

The *preservation* of infusions has been the subject of considerable unnecessary writing. By the very character of preparation, no attempts should be made to preserve infusions, which should be freshly prepared as required. The addition of any preservative agent to infusions is, of course, out of the question. In England, where the infusions are used very largely, a separate counter is arranged for the use of infusions, and here are placed a line of infusion mugs. At the beginning of each day the contents of these mugs are thrown away, and the apparatus carefully washed, and new quantities of the infusions are prepared. No infusion should be dispensed later than twenty-four hours after making.

SPECIAL NOTES ON OFFICIAL INFUSIONS

INFUSA—Infusions

Condensed Recipe.

This is a general formula directing that unless otherwise specified, an infusion should be made by moistening 50 Gm. of the coarsely comminuted drug in a suitable vessel, preferably of earthenware and provided with a cover, with 50 cc. cold water and allowing to stand fifteen minutes, then adding 900 cc. of boiling water and allowing to stand for one-half hour, straining the mixture, and washing the strainer with enough water to make 1 liter. For details, see U.S.P., p. 194.

An infusion may be dispensed only if it has been recently prepared. If the drug concentration of an infusion is not otherwise specified, it is to be prepared according to the general formula given above.

Caution.—The drug concentration of an infusion representing a potent drug should be specified by the physician.

Remarks.—A "general formula" is an attempt to furnish a recipe for the manufacture of every representative of that particular line of preparations, the infusions, unless a special recipe is given by the Pharmacopœia or by the physician, or unless the active ingredient is so potent that the preparation so made is dangerous.

Thus, a prescription for any infusion, save digitalis, gentian compound, and senna compound (for which recipes are given in the National Formulary), or some very powerful drug, is expected to be compounded by the pharmacist according to the general formula. Thus a prescription for 1000 cc. infusion of buchu is to be prepared by macerating 50 Gm. of the bruised drug with 900 cc. boiling water after macerating with 50 cc. of cold water and for any quantity the same proportion of buchu to boiling water (5 : 100) is to be preserved.

Infusum Digitalis (U.S.P. X; N.F. VI) or *Infusion of Digitalis* is prepared by pouring 900 cc. boiling water upon powdered digitalis, 15 Gm., adding alcohol in which spirit of cinnamon has been dissolved and finally enough water to make a liter. Infusion of digitalis contains 1½ per cent of digitalis leaves, the strength of which is extracted by maceration with boiling water. As in the case of digitalis itself (p. 719) there is much controversy as to the therapeutic value of the infusion. Hatcher and Eggleston claim that an infusion seven days old is as potent as a fresh sample, whereas Pomeroy and Heyl state that the infusion should be thrown out after five days: Hatcher and Weiss find no difference in the therapeutic action of this infusion and of tincture of digitalis except that the infusion has about one seventh the therapeutic efficiency of the tincture. Hintzelmann and Joachimoglu state that alkaline infusions deteriorate more rapidly than neutral or acid samples, whereas Tainter believes that the degree of acidity (pH) has little influence on the physiologic activity of the infusion. Otto advises a rapid cooling of the finished infusion in order to lessen the danger of hydrolysis of the unstable glucosides. It has been determined that infusion of digitalis which has been sterilized and well sealed keeps for two years and that the addition of 0.3 per cent chloroform or 0.06 per cent thymol will keep it under ordinary conditions for three weeks. For other references see Bibliography at the end of this chapter.

Dose.—6 cc. (1½ fluidrachms).

Infusion Sennæ Cum Magnesii Sulfate (U.S.P. IX; N.F. VI) or *Compound Infusion of Senna* is made by infusing 60 Gm. of senna, 120 Gm. of manna and 20 Gm. of fennel with 800 cc. of boiling water for one-half hour. After straining and expression, 120 Gm. of magnesium sulfate are dissolved in the liquid and then enough water is added to make 1 liter. This preparation is that old remedy, "senna, manna, and salts," with a bit of fennel added for flavor. Its synonym is *black draught.* This must not be confounded with "black drop" (p. 277), as it has been in the past, with fatal results.

INFUSIONS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 mils).	Remarks.
Infusum digitalis.	Infusion of digitalis.	Digitalis, 15 Gm ; alcohol, spirit of cinnamon; distilled water.	*Dose.*—6 cc. (1½ fluidrachms).
Infusum gentianæ compositum.	Compound infusion of gentian.	Gentian, 30 Gm ; coriander; bitter orange peel; diluted alcohol. Make a tincture and dilute with water.	*Dose.*—15 cc. (4 fluidrachms). The percolate or concentrate infusion may be preserved in well-closed containers but the infusion must not be dispensed unless it has been recently prepared.
Infusum sennæ cum magnesii sulfate.	Infusion of senna with magnesium sulfate; compound infusion of senna.	....	See above.

DECOCTIONS

These are *liquids made by boiling the drug for fifteen minutes or longer with water.*

The boiling should not be carried on in iron vessels, as a large number of drugs from which decoctions are made contain tannin, and this, combining with iron, forms a black mixture (ink). In Germany and other countries where the decoctions are popular they are prepared in special block-tin vessels; but in America, where the decoctions are but seldom prescribed, an enameled dish will answer the purpose.

Neither the present Pharmacopœia nor the National Formulary recognize any specific decoctions. The U.S.P. gives the general formula, outlined below.

DECOCTA—Decoctions

Condensed Recipe.

A general formula directing the boiling of 50 Gm. of coarsely comminuted drug with 1000 cc. of water for fifteen minutes. Cool, express, strain, and wash strainer with enough cold water to make 1 liter. For details, see U.S.P., p. 134.

A decoction may be dispensed only if it has been recently prepared. In case the drug concentration of a decoction is not otherwise specified, it is to be prepared in accordance with the general formula.

Remarks.—The comments made regarding the general formula for infusions apply with equal force at this place.

The two decoctions recognized by the Pharmacopœia of 1890 are worthy of the mention given on the next page.

Decoctum Cetrariæ (U.S.P. 1890) is made by macerating 50 Gm. cetraria with 400 cc. cold water for a half-hour and then the expressed liquid thrown away. The washed cetraria was then boiled with 1000 cc. water for fifteen minutes.

Cetraria, or Iceland moss, contains a bitter principle, called cetraric acid, as well as the mucilage, the constituent which makes the decoction a nutritious jelly. The presence of this bitter principle in the jelly would render it distasteful. Fortunately, however, cetraric acid is soluble in *cold* water, and for this reason the drug is first macerated in cold water, in which the cetraric acid will dissolve, this bitter liquid expressed and thrown away; then, and only then, can the cetraria be boiled to a jelly, free from bitterness.

Decoctum Sarsaparillæ Compositum (N.F. IV) made by boiling 100 Gm. bruised sarsaparilla and 20 Gm. guaiacum wood for a half hour with 1000 cc. water, then adding 20 Gm. sassafras bark, 20 Gm. glycyrrhiza, and 10 Gm. mezereum, and letting it macerate two hours. To the strained liquid enough water was added to make 1000 cc.

This decoction, rarely used in this country, is popular in Germany as an alterative. It is called Zittmann's decoction.

TINCTURES

Tinctures have been defined as *alcoholic solutions of nonvolatile substances* obtained by extraction of drugs.

An exception to the statement "alcoholic solutions of nonvolatile substances" is found in tincture of iodine. The active ingredient of this is the volatile solid, iodine; but the presence of potassium iodide which is nonvolatile brings the tincture practically within the definition given above. The present pharmacopœial definition for tinctures is "alcoholic or hydro-alcoholic solutions of the active principles of animal or vegetable drugs."

Tinctures prepared from drugs differ from fluidextracts in the matter of strength. All fluidextracts, as we will learn later (p. 259), are adjusted to represent a 100 per cent product, that is, 100 cc. represent the active principles of 100 Gm. of a standard drug, while the tinctures are much weaker, none of those official being stronger than 50 per cent. The strength of tinctures varies, ranging from camphorated tincture of opium, which contains but 0.4 of 1 per cent opium, its active ingredient, to the two 50 per cent tinctures; lemon peel and sweet orange. In conformity with the recommendations of the International Protocol as adopted at Brussels, and with international standards, the tinctures of potent drugs represent 10 Gm. of the drug in each 100 cc. of tincture.

The following table gives the strength of every tincture recognized by the present Pharmacopœia and National Formulary.

STRENGTH OF OFFICIAL TINCTURES

0.4 *of* 1 *per cent*	Tinctures of antimony (N.F. VI) and opium, camphorated (0.4 of 1 per cent opium, 1.6 per cent total active constituents).
1.5 *per cent*	Tincture of cudbear, compound (N.F. VI).
2 *per cent*	Tincture of iodine, mild (also 2.3 per cent sodium iodide).
5 *per cent*	Tincture of iodides (N.F. VI) (also 2.5 per cent potassium iodide).
7 *per cent*	Tincture of iodine (also 5 per cent potassium iodide).
10 *per cent*	Tinctures of aconite, belladonna, cannabis (N.F. VI) cantharides, capsicum, cocculus (N.F. VI), colchicum seed, cudbear (N.F. VI), digitalis, gelsemium (N.F. VI), hyoscyamus, ipecac (N.F. VI), ipecac and opium (N.F. VI), larkspur (N.F. VI), larkspur (N.F. VI), larkspur, acetic (N.F. VI), lobelia (N.F. VI), nux vomica, opium, pulsatilla (N.F. VI), sanguinaria (N.F. VI), squill, stramonium, strophanthus (N.F. VI), and veratrum viride.

16.5 *per cent*	Tincture of iodine, stronger (N.F. VI) (also 3.5 per cent potassium iodide).
20 *per cent*	Tinctures of arnica (N.F. VI), asafetida (N.F. VI), benzoin, bitter orange peel, bryonia (N.F. VI), calendula (N.F. VI), calumba (N.F. VI), cimicifuga (N.F. VI), cinnamon (N.F. VI), cubeb (N.F. VI), guaiac (N.F. VI), guaiac, ammoniated (N.F. VI), hydrastis (N.F. VI), jalap (N.F. VI), kino, myrrh, nutgall (N.F. VI), quassia (N.F. VI), quillaja (N.F. VI), serpentaria (N.F. VI), tolu balsam, valerian, and valerian, ammoniated (N.F. VI).
40 *per cent*	Tincture of colchicum corm, strong (N.F. VI).
50 *per cent*	Tinctures of cactus grandiflorus (N.F. VI), lemon and sweet orange peel.

Some official tinctures do not adapt themselves to the table just given, so must be given special mention.

Tincture of ferric citrochloride (N.F. VI)	represents 35 per cent solution of ferric chloride or 4.48 per cent iron, 80 per cent total active constituents.
Tincture of ferric chloride	represents 35 per cent solution of ferric chloride or 4.5 per cent iron.
Tincture of lavender, compound	represents 0.8 per cent oil of lavender and 5.5 per cent total active constituents.

The remaining official tinctures adjust themselves to the following table of strengths:

Name of Tincture	*Percentage of Principal Constituent*	*Percentage of Total Active Constituents*
Tincture of aloe (N.F. VI)	10	30
Tincture of aloe and myrrh (N.F. VI)	10	30
Tincture of benzoin, compound	10	24
Tincture of capsicum and myrrh	3	15
Tincture of cardamom, compound	2	6.2
Tincture of cinchona, compound	10	20
Tincture of gambir, compound (N.F. VI)	20	30
Tincture of gentian, compound	10	15
Tincture of rhubarb, aromatic	20	30
Tincture of rhubarb, compound (N.F. VI)	20	23
Tincture of rhubarb, sweet (N.F. VI)	10	19
Tincture of vanilla (N.F. VI)	10	30
Tincture of viburnum, compound (N.F. VI)	3.5	19.5

Explaining the foregoing, let it be said that by "principal constituent" is meant the drug giving the compound tincture its name, and as to "total active constituents" these will be enumerated in the proper place.

Attention should be called to the distinction between "represents" and "contains"; thus, it can be said that tincture of vanilla, N.F., "represents 10 per cent vanilla and contains 20 per cent sugar." This distinction should always be borne in mind in discussing the strength of liquid pharmaceuticals, and it can only be said of any one of these that it "contains" a certain percentage of a drug when that drug is completely dissolved in the liquid, as in the case of the sugar in tincture of vanilla. If the drug is composed of vegetable tissue not entirely soluble in the menstruum, as in the case of the vanilla, then the tincture does not "contain" 10 per cent vanilla, but merely "represents" the active principles obtained from 10 per cent vanilla by extraction. There is another clumsy phase in the glib statement that a certain tincture is 10 per cent; namely, a true 10 per cent preparation is one in which all the ingredients are weighed, that is, represents 10 Gm. of drug in 100 Gm. of the finished product. On the other hand, a 10 per cent tincture contains the activity of 10 Gm. of drug in 100 cc. of finished tincture. This, however, is a question of "splitting hairs," since in making the greater number of the liquid pharmaceuticals of the Pharmacopœia the solids are weighed, while the preparation is finished by bringing it to a certain volume. Further attention must be called to the fact that the ultimate strength of many of the official tinctures is not based on percentage of drug represented but upon its chemical or biological assay.

The following tables give lists of official tinctures arranged according to method of manufacture. In passing, it may be said that all of them are galenic preparations.

OFFICIAL TINCTURES MADE BY SOLUTION OR DILUTION

Preparation	*Solvent*
Tincture of antimony (N.F. VI)	Alcohol, 200 cc.; water, approximately 800 cc.
Tincture of ferric citrochloride (N.F. VI)	Alcohol, 150 cc.; solution of ferric chloride, 350 cc.; water, approximately 500 cc.
Tincture of ferric chloride	Alcohol, 650 cc.; solution of ferric chloride, 350 cc.
Tincture of iodides (N.F. VI)	Alcohol, approximately 500 cc.; stronger ammonia water, 100 cc.; water, 400 cc.
Tincture of iodine	Alcohol, approximately 950 cc.; water, 50 cc.
Tincture of iodine, mild	Diluted alcohol.
Tincture of iodine, stronger (N.F. VI)	Alcohol, approximately 750 cc.; water, 250 cc.

OFFICIAL TINCTURES MADE FROM FLUIDEXTRACTS (DILUTION)

Preparation	*Diluent*
Tincture of colchicum corm, strong (N.F. VI)	Alcohol, 50 cc.; water, 550 cc.
Tincture of ipecac (N.F. VI)	Alcohol, 200 cc.; water, 685 cc.; diluted hydrochloric acid, 15 cc.

OFFICIAL TINCTURES MADE FROM TINCTURES (DILUTION)

Preparation	*Diluent*
Tincture of cudbear, compound (N.F. VI)	Alcohol, 150 cc.; water, approximately 600 cc.
Tincture of ipecac and opium (N.F. VI)	Diluted alcohol.

OFFICIAL TINCTURES MADE BY MACERATION

Menstruum	*Preparation*
Alcohol, U.S.P.	Tincture of asafetida (N.F. VI). Tincture of benzoin. Tincture of benzoin, compound. Tincture of cactus grandiflorus (N.F. VI). Tincture of guaiac (N.F. VI). Tincture of lemon. Tincture of myrrh. Tincture of sweet orange peel. Tincture of tolu balsam.
Alcohol, 750 cc.; water, 250 cc.	Tincture of aloe and myrrh (N.F. VI). Tincture of lavender, compound.
Diluted alcohol, U.S.P.	Tincture of aloe (N.F. VI).
Diluted alcohol, 600 cc.; alcohol, 200 cc.; water, 200 cc.	Tincture of vanilla (N.F. VI).
Glycerin, 100 cc.; alcohol, 900 cc	Tincture of kino.
Glycerin, 50 cc.; diluted alcohol, 950 cc.	Tincture of cardamom, compound.
Glycerin, 40 cc.; diluted alcohol, 950 cc.	Tincture of opium, camphorated.
Glycerin, 50 cc.; acetic acid, 50 cc.; alcohol, 100 cc.; water, 800 cc.	Tincture of larkspur, acetic (N.F. VI).
Aromatic spirit of ammonia	Tincture of guaiac, ammoniated (N.F. VI).

OFFICIAL TINCTURE MADE BY INFUSION

Menstruum	*Preparation*
Alcohol, 350 cc.; water, 650 cc.	Tincture of quillaja (N.F. VI).

OFFICIAL TINCTURES MADE BY PERCOLATION

Menstruum	*Preparation*
Alcohol, U.S.P.	Tincture of calendula (N.F. VI).
	Tincture of cannabis (N.F. VI).
	Tincture of larkspur (N.F. VI).
	Tincture of strophanthus (N.F. VI).
	Tincture of veratrum viride.
Alcohol, 900 cc.; water, 100 cc.	Tincture of bryonia (N.F. VI).
	Tincture of capsicum.
	Tincture of capsicum and myrrh (N.F. VI).
	Tincture of cimicifuga (N.F. VI).
	Tincture of cubeb (N.F. VI).
	Tincture of jalap (N.F. VI).
Alcohol, 800 cc.; water, 200 cc.	Tincture of digitalis.
	Tincture of gelsemium (N.F. VI).
	Tincture of serpentaria (N.F. VI).
Alcohol, 750 cc.; water, 250 cc.	Tincture of aconite.
	Tincture of arnica (N.F. VI).
	Tincture of belladonna.
	Tincture of cinnamon (N.F. VI).
	Tincture of cudbear (N.F. VI).
	Tincture of hyoscyamus.
	Tincture of pulsatilla (N.F. VI).
	Tincture of squill.
	Tincture of stramonium.
	Tincture of valerian.
Alcohol, 600 cc.; water, 400 cc.	Tincture of bitter orange peel.
	Tincture of colchicum seed.
	Tincture of calumba (N.F. VI).
	Tincture of hydrastis (N.F. VI).
Alcohol, 400 cc.: water, 600 cc.	Tincture of quassia (N.F. VI).
Alcohol, 200 cc.; water, 800 cc.	Tincture of opium.
Diluted alcohol, U.S.P.	Tincture of cocculus (N.F. VI).
Glycerin, 100 cc.; alcohol, 900 cc.	Tincture of gambir, compound (N.F. VI).
	Tincture of nutgall (N.F. VI).
Glycerin, 100 cc.; alcohol, 500 cc.; water, 400 cc.; diluted alcohol	Tincture of gentian, compound.
	Tincture of rhubarb, aromatic.
	Tincture of rhubarb, compound (N.F. VI).
	Tincture of rhubarb, sweet (N.F. VI).
Glycerin, 100 cc.: alcohol, 500 cc.; water, 400 cc.	Tincture of gentian, compound.
Glycerin, 75 cc.; alcohol, 750 cc.; water, 175 cc.	Tincture of viburnum, compound (N.F. VI).
Acetic acid, 5 cc.; diluted alcohol, 995 cc.	Tincture of lobelia (N.F. VI).
Glacial acetic acid, 100 cc.; alcohol, 900 cc.	Tincture of cantharides.
Hydrochloric acid, 10 cc.; alcohol, 675 cc.; water, 315 cc.	Tincture of sanguinaria (N.F. VI).
Diluted hydrochloric acid, 15 cc.; alcohol, 660 cc.; water, 315 cc.	Tincture of cinchona, compound.
Diluted hydrochloric acid, 7.5 cc.; alcohol, 750 cc.; water, 242.5 cc.	Tincture of nux vomica.
Aromatic spirit of ammonia	Tincture of valerian, ammoniated (N.F. VI).

As to the three principal methods of preparing tinctures given in the table, no better explanation can be given than that provided in the general formulas which are outlined in the present Pharmacopœia, which the student should carefully read. See U.S.P., page 390. The official maceration process is designated as Process M and the official percolation process as Process P.

In percolating tinctures containing glycerin it is customary to use the menstruum specified above as a primal menstruum and at the end of the process to use mixtures of alcohol and water.

Precipitation in tinctures and in fluidextracts (p. 263) is a source of much annoyance. Scoville (1927) studied precipitation in the tinctures of 31 typical drugs: (*a*) alkaloidal, (*b*) astringent; (*c*) cathartic; and (*d*) miscellaneous. These were subjected to differences in light, acidity, alkalinity, oxidation, reduction, ionizing, and dehydrating agents and buffers of the stabilizers studied, he found glycerin and ethanol most effective as stabilizing agents for use in menstrua.

STORAGE OF TINCTURES

Tinctures should be stored in tightly-stoppered containers and should not be exposed during storage to direct sunlight or to temperatures above the normal temperature of living rooms.

TINCTURÆ—Tinctures

Condensed Recipe.

This is a general formula outlining the manufacture of tinctures by percolation and by maceration. For details, see U.S.P., p. 390.

Remarks.—Tinctures are prepared by maceration only when percolation is not advisable. This is the case with a resinous drug which if packed in a percolator and treated with alcohol would become a sticky mass, clogging the percolator. With such a drug percolation is only possible, if it is mixed with more than its own weight of clean dry sand. As to the choice of menstrua, this was already discussed on p. 188, so here it need only be said, on comparison of the above table of menstrua with the discussion of the chemical constituents of the drugs employed, found in Part IV, that the drugs requiring strong alcohol for extraction are those grouped among resins, gum resins, oleoresinous, or volatile oil drugs; that those extracted with glycerinic menstruum are tannin-bearing drugs; that those having acetic acid in the menstruum are drugs containing volatile alkaloids; while the ordinary drugs containing glucosides, neutral principles, or stable alkaloids are extracted with alcohol more or less diluted with water.

It is generally considered improper to prepare a tincture by diluting a fluidextract. Davy calling such tinctures "questionable." On the other hand, Scoville defends the custom.

There are 30 tinctures recognized by the present Pharmacopœia—10 less than were recognized by U.S.P. X and 24 less than were included in the U.S.P. IX.

SPECIAL NOTES ON OFFICIAL TINCTURES

TINCTURA ACONITI—Tincture of Aconite

(Tr. Aconit.—Aconiti tinctura P.I.)

Tincture of Aconite, when assayed by the method directed (see U.S.P., p. 391), possesses a potency, per cubic centimeter, equivalent to not less than 0.14 mg. and not more than 0.16 mg. of reference aconitine.

Alcohol Content.—65 to 70 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of drug in No. 60 powder with a sufficient amount of the menstruum—alcohol, 3 volumes; water, 1 volume; macerate for twenty-four hours after packing and percolate until 950 cc. of tincture are obtained. A part of this is assayed and the rest is adjusted to the official strength and *p*H, by addition of the menstruum mentioned above and sufficient hydrochloric acid. For details, see U.S.P., p. 391.

Remarks.—Swanson advised the addition of a small amount of either hydrochloric or acetic acid to this tincture in order to prevent the hydrolysis of the potent aconitine to almost inert aconine. The official method prescribes hydrochloric acid for the purpose. The tincture is assayed biologically using the guinea pig method. A tolerance of 20 per cent above or below the standard is permitted because of variable factors. See U.S.P., page 391.

Dose.—0.6 cc. (10 minims).

TINCTURA AURANTII AMARI—Tincture of Bitter Orange Peel

(Tr. Aurant. Amar.)

Alcohol Content.—58 to 62 per cent by volume.

Condensed Recipe.

Moisten 200 Gm. of drug in No. 40 powder with a sufficient amount of the menstruum; alcohol, 2 volumes; water, 1 volume; macerate twenty-four hours after packing and then percolate to 1000 cc. For details, see U.S.P., p. 392.

Dose.—4 cc. (1 fluidrachm).

TINCTURA AURANTII DULCIS—Tincture of Sweet Orange Peel

(Tr. Aurant. Dulc.)

Alcohol Content.—73 to 76 per cent by volume.

Condensed Recipe.

Five hundred Gm. freshly grated sweet orange peel are macerated with 1000 cc. of alcohol for three days, after which the mixture is filtered, the filter being washed with enough alcohol to make 1 liter. For details, see U.S.P., p. 392.

Remarks.—This tincture is a pleasant flavor, more like a spirit than a tincture.

Dose.—4 cc. (1 fluidrachm).

TINCTURA BALSAMI TOLUTANI—Tincture of Tolu Balsam

(Tr. Balsam. Tolu.—Tinctura Tolu, U.S.P. X, Tolu Tincture)

Alcohol Content.—80 to 85 per cent by volume.

Condensed Recipe.

Macerate 200 Gm. balsam of tolu with enough alcohol to make 1000 cc. For details see U.S.P., page 393.

Remarks.—Unlike benzoin and other resinous drugs from which tinctures are prepared, tolu is almost completely soluble in alcohol; hence the manufacture might be considered as one of solution rather than as one of maceration. The tincture is used in making the official *Syrup of Tolu* (p. 219).

Dose.—2 cc. (30 minims).

TINCTURA BELLADONNÆ—Tincture of Belladonna

(Tr. Bellad.—Tinctura Belladonnæ Foliorum, Tinctura Belladonnæ P.I.)

Tincture of Belladonna yields, from each 100 cc., not less than 0.027 Gm. and not more than 0.033 Gm. of the alkaloids of belladonna leaf.

Alcohol Content.—65 to 70 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of drug in No. 40 powder with the menstruum; alcohol, 3 volumes; water, 1 volume; macerate and percolate to 1000 cc. For details, see U.S.P., p. 393.

Remarks.—This tincture is assayed chemically. See U.S.P., pages 393 and 194. The belladonna alkaloids are sometimes referred to as mydriatic alkaloids. The physiological activity of this tincture may be tested by the mydriatic effect upon the pupil of a cat's eye.

Dose.—0.6 cc. (10 minims).

TINCTURA BENZOINI—Tincture of Benzoin

(Tr. Benz.)

Alcohol Content.—75 to 83 per cent by volume.

Condensed Recipe.

Macerate 200 Gm. of benzoin in No. 40 powder with enough alcohol to make 1000 cc. Details as in making tincture of tolu balsam. See U.S.P., p. 393.

Remarks.—Tincture of benzoin and compound tincture of benzoin are now used largely in steam inhalers for bronchial troubles.

Dose.—1 cc. (15 minims).

TINCTURA BENZOINI COMPOSITA—Compound Tincture of Benzoin

(Tr. Benz. Co.)

Alcohol Content.—74 to 80 per cent by volume.

Condensed Recipe.

Ingredients.—Benzoin, in No. 40 powder, 100 Gm.; aloes, in No. 40 powder, 20 Gm.; storax, 80 Gm.; balsam of tolu, 40 Gm.; alcohol, enough to make 1 liter. Macerate as in making tincture of tolu balsam. See U.S.P., p. 393.

Remarks.—This useful preparation is similar to, but not identical with, the old-time proprietaries: *Turlington's balsam, elixir commendatoris, baume de commandeur and friars' balsam.* The latter product contained balsam of Peru, myrrh, and angelica root, in addition to the ingredients of the official tincture. It is the custom in this country to dispense compound tincture of benzoin on calls for the preparations whose synonyms have just been given.

This preparation, which has enjoyed popularity for two centuries or more, was regarded with scepticism by medical authorities ten years ago. Macht's pharmacological studies of benzyl compounds (p. 797), however, show that the benzoin preparations have distinct therapeutic value.

Dose.—2 cc. (30 minims).

TINCTURA CANTHARIDIS—Tincture of Cantharides

(Tr. Canthar.—Tinctura cantharidis P.I.)

Alcohol Content.—78 to 84 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of drug in a No. 80 powder with 100 cc. of glacial acetic acid and 100 cc. of alcohol; macerate four days in a warm place and then percolate with alcohol to 1000 cc. For details, see U.S.P., p. 394.

Remarks.—There has been much experimentation as to the proper method of securing a complete extraction of cantharidin in making this tincture. The process of U.S.P. XI differs slightly from that of U.S.P. X and these differ from the U.S.P. IX process where digestion with alcohol between 50° and 55° C. was directed. The work of Nitardy indicated the value of acetic acid as a solvent for the cantharidin and this idea was adopted in the last Pharmacopœia and the amount of acetic acid was doubled in the present formula.

Tincture of cantharides is largely used as a scalp stimulator in hair dressings.

Dose.—0.1 cc. (1½ minims).

TINCTURA CAPSICI—Tincture of Capsicum

(Tr. Capsic.)

Alcohol Content.—80 to 85 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of the drug in No. 40 powder with the menstruum—9 volumes of alcohol; 1 volume of water; macerate and then percolate to 1000 cc. For details see U.S.P., p. 394.

Remarks.—The Pharmacopœia provides an interesting "organoleptic test" for this tincture; a test based upon the burning pungent sensation produced in the mouth and throat upon swallowing a highly diluted sweetened aqueous solution of the tincture. See U.S.P., page 395.

Dose.—0.5 cc. (8 minims).

TINCTURA CARDAMOMI COMPOSITA—Compound Tincture of Cardamom

(Tr. Cardam. Co.)

Alcohol Content.—45 to 47 per cent by volume.

Condensed Recipe.

Macerate 20 Gm. cardamom seed in No. 40 powder; 25 Gm. cinnamon in No. 60 powder; 12 Gm. caraway in No. 40 powder; and 5 Gm. cochineal in No. 60 powder, with the menstruum—glycerin, 50 cc.; diluted alcohol, 950 cc.; finally using enough diluted alcohol to make 1000 cc. For details see U.S.P. XI, p. 395.

Remarks.—A mnemonic for the active constituents of this compound tincture are the four C's:

Cardamom
Cinnamon
Caraway
Cochineal

This bright-red liquid—the color due to the cochineal—is a pleasant aromatic and carminative. Variation in the color of different lots of this tincture has been ascribed to differences in *p*H. This is said to vary from 4.4 to 5.

Dose.—4 cc. (1 fluidrachm).

TINCTURA CINCHONÆ COMPOSITA—Compound Tincture of Cinchona

(Tr. Cinch. Co.)

Compound Tincture of Cinchona yields, from each 100 cc., not less than 0.4 Gm. and not more than 0.5 Gm. of the alkaloids of cinchona.

Alcohol Content.—56 to 62 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. cinchona in No. 40 powder, 80 Gm. bitter orange peel in No. 40 powder, and 20 Gm. serpentaria in No. 60 powder, with a mixture of 130 cc. of alcohol, 15 cc. of diluted hydrochloric acid, and 50 cc. of distilled water; macerate and percolate, completing the percolation with a mixture of 2 volumes of alcohol and 1 volume of distilled water collecting 925 cc. of percolate. Add 75 cc. of glycerin and mix well. Adjust with a mixture of alcohol 20 volumes, glycerin, 2.5 volumes, diluted HCl 0.5 volumes, and water, 7 volumes to the official alkaloid content.

Remarks.—A chemical assay is prescribed for this tincture. See U.S.P., page 396. This is sometimes called *Huxham's tincture of bark*, and is a valuable tonic. It should not be dispensed with iron preparations, since the cinchotannic acid present in the bark reacts with iron to form an inky mixture. The addition of glycerin to the tincture after percolation reduces the amount of tannin extracted during percolation. Formerly the glycerin was a part of the extracting menstruum.

Dose.—4 cc. (1 fluidrachm).

TINCTURA COLCHICI SEMINIS—Tincture of Colchicum Seed

(Tr. Colch. Sem.—Tinctura Colchici U.S.P. X, Tinctura Colchici P.I.)

Tincture of Colchicum Seed yields, from each 100 cc., not less than 0.036 Gm. and not more than 0.044 Gm. of colchicine.

Alcohol Content.—59 to 63 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of the drug in a No. 40 powder with the menstruum—alcohol, 2 volumes; water, 1 volume; macerate and then percolate to 1000 mils. For details see U.S.P., p. 396.

Remarks.—This tincture is assayed chemically, following the process described under assay of the drug. See U.S.P., pages 397 and 128. The N.F. recognizes a "strong tincture of colchicum corm" which replaces the former "wine of colchicum corm." It contains 0.125 to 0.155 Gm. colchicine per 100 cc.

Dose.—2 cc. (30 minims).

TINCTURA DIGITALIS—Tincture of Digitalis

(Tr. Digit.—Tinctura Digitalis P.I.)

The potency of Tincture of Digitalis shall be such that 1 cc. of the tincture, when assayed as directed, shall possess an activity equivalent to not less than 1 and not more than 1.1 U.S.P. digitalis units. (See U.S.P., p. 136.)

Alcohol Content.—67 to 72 per cent by volume.

Condensed Recipe.

Digitalis (100 Gm.) in No. 60 powder is percolated with the menstruum—alcohol 4 volumes; water 1 volume. Percolate is assayed biologically and is diluted to official strength with the menstruum. For details, see U.S.P., p. 397.

Remarks.—Of late years, efforts have been made to popularize a fat-free tincture of digitalis and the U.S.P. X provided for defatting the drug by percolation with petroleum benzin. This proved to be unsatisfactory and unnecessary refinement as it could not be proved that the fat in the digitalis leaf had any untoward effect. This tincture is assayed biologically using frogs as the test animal. Various test animals have been proposed, notably guinea pigs and cats. A system of standardization based on "cat units" has been worked out but has not been made official. Considerable work has been done on the assay of digitalis preparations and apparently much remains to be done. Owing to the many variable factors in digitalis standardization a tolerance of 20 per cent above or below the official standard is permitted. For complete assay, see U.S.P., page 397.

Hatcher's work on the relative value of tincture and infusion of digitalis is discussed on p. 237. Krantz finds that this tincture should be faintly acid and that samples stored in flint bottles in the dark showed practically no change in *p*H value during one year.

Dose.—1 cc. (15 minims).

TINCTURA FERRI CHLORIDI—Tincture of Ferric Chloride

This preparation can best be discussed among the salts of iron. (See p. 566.)

TINCTURA GENTIANÆ COMPOSITA—Compound Tincture of Gentian

(Tr. Gentian Co.)

Alcohol Content.—43 to 47 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. gentian, 40 Gm. bitter orange peel, and 10 Gm. cardamom seed all in a No. 40 powder, with the menstruum—glycerin, 100 cc.; alcohol, 500 cc.; water, 400 cc.; macerate and then percolate, using diluted alcohol as the last menstruum. For details, see U.S.P., p. 399.

Dose.—4 cc. (1 fluidrachm).

TINCTURA HYOSCYAMI—Tincture of Hyoscyamus

(Tr. Hyosc.—Tincture of Henbane, Tinctura Hyoscyami P.I.)

Tincture of Hyoscyamus yields, from each 100 cc., not less than 0.0034 Gm. and not more than 0.0046 Gm. of the alkaloids of hyoscyamus.

Alcohol Content.—65 to 69 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of the drug in a No. 40 powder with the menstruum; alcohol, 3 volumes; water, 1 volume; macerate and then percolate to 1000 cc. Finally adjust the tincture to the required alkaloid content.

Remarks.—A chemical assay is directed for this tincture. The alkaloid content is determined by a method described on pages 400 and 194 of the U.S.P.

Dose.—2 cc. (30 minims).

TINCTURA IODI—Tincture of Iodine

This important official will be discussed under Iodine (p. 427).

TINCTURA IODI MITIS—Mild Tincture of Iodine

(Tr. Iodi Mit.)

Mild Tincture of Iodine contains, in each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of I and not less than 2.1 Gm. and not more than 2.5 Gm. of NaI.

Storage.—Preserve in glass bottles, closed with stoppers resistant to corrosion, and in a cool place, protected from light.

Alcohol Content.—44 to 48 per cent by volume.

Condensed Recipe.

Dissolve iodine, 20 Gm.; sodium iodide, 23 Gm. in sufficient diluted alcohol (U.S.P.) to make 1000 cc.

Description.—Reddish-brown transparent liquid with odor of iodine.

Identity.—See U.S.P., p. 401.

Assay.—See U.S.P., pp. 402 and 214.

Remarks.—This mild tincture of iodine has been made official to supply a less irritating iodine solution than the 7 per cent tincture. It is claimed that a 2 per cent tincture is antiseptic and thus suitable for ordinary "first-aid" purposes. Sodium iodide is used in this tincture in place of potassium iodide (as in the 7 per cent tincture, because it is just as satisfactory in aiding solution of the iodine and it is claimed to be less irritating to tissues than the potassium salt. It is not intended for internal use, hence no dose is given.

TINCTURA KINO—Tincture of Kino

(Tr. Kino)

Note.—This tincture has been doubled in strength to make it conform to the P.I. recommendation for nonpotent tinctures. Its dose is therefore one half that of the U.S.P. X dose.

Storage.—Preserve in a cool, dark place, in small tightly-stoppered, completely-filled bottles.

Alcohol Content.—76 to 82 per cent by volume.

Condensed Recipe.

Macerate 200 Gm. of kino with the menstruum—alcohol, 9 volumes; glycerin, 1 volume during three days, then filter and wash residue on filter with enough menstruum to make 1000 cc. For details, see U.S.P., p. 402.

Remarks.—Previous to the U.S.P. X tincture of kino had to be kept in small well-stoppered and completely filled bottles; else it gelatinized. It was found that this gelatinization was due to an enzyme, which can be destroyed by heat, hence the direction in the U.S.P. X recipe to heat the drug with water on a water bath for an hour and adding alcohol, macerating, decanting, and straining. In the present formula the extraction process is changed to maceration with a strongly alcoholic menstruum containing glycerin.

Dose.—2 cc. (30 minims).

TINCTURA LAVANDULÆ COMPOSITA—Compound Tincture of Lavender

(Tr. Lavand. Co.—Compound Spirit of Lavender)

Alcohol Content.—67 to 72 per cent by volume.

Condensed Recipe.

Macerate 20 Gm. cinnamon; 5 Gm. clove; 10 Gm. myristica and 10 Gm. red saunders, all in No. 40 powder, with the menstruum—alcohol, 750 cc.; oil of lavender, 8 cc.; oil of rosemary, 2 cc.; water, 250 cc. Complete the preparation with a menstruum consisting of alcohol, 3 volumes; water, 1 volume. For details, see U.S.P., p. 402.

Remarks.—This tincture is sometimes called "red lavender," because of its brilliant color, due to the red saunders it contains. It has a reputation among household remedies as being good in "heart trouble," although, in truth, its only value is to relieve flatulence.

Dose.—2 cc. (30 minims).

TINCTURA LIMONIS—Tincture of Lemon

(Tr. Limon.—Tinctura Limonis Corticis)

Alcohol Content.—70 to 75 per cent by volume.

Condensed Recipe.

This is a 50 per cent alcoholic extract of fresh lemon peel, made exactly as tincture of sweet orange peel. For details see U.S.P., page 403.

Remarks.—Tincture of lemon peel replaces *spirit of lemon* of the Pharmacopœia of 1890. It is used entirely as a flavor, hence no dose is given.

TINCTURA MYRRHÆ—Tincture of Myrrh

(Tr. Myrrh)

Alcohol Content.—83 to 88 per cent by volume.

Condensed Recipe.

Macerate 200 Gm. of the drug in a No. 40 powder with enough menstruum—alcohol (U.S.P.)—to make 1000 cc. For details see U.S.P., page 403.

Remarks.—Myrrh (see p. 877) contains a larger percentage of gummy matter than asafetida, and this gum, which does not dissolve in the strong alcoholic menstruum and which is left on the filter, after making the tincture, has been suggested as a source of label mucilage.

The tincture is used considerably in mouth washes and is not often given internally.

Dose.—2 cc. (30 minims).

TINCTURA NUCIS VOMICÆ—Tincture of Nux Vomica

(Tr. Nuc. Vom.—Tinctura Strychni P.I.)

Tincture of Nux Vomica yields, from each 100 cc., not less than 0.108 Gm. and not more than 0.120 Gm. of strychnine.

Alcohol Content.—67 to 72 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of the drug in a No. 40 powder, with the menstruum—hydrochloric acid, 7.5 cc.; alcohol, 50 cc.; water, 42.5 cc.; macerate and then percolate to 950 cc.; using as menstruum, alcohol, 3 volumes; water, 1 volume. Adjust the volume of finished tincture with a mixture of 0.75 cc. hydrochloric acid, 75 cc. alcohol, and 24.25 cc. water to yield the required amount of alkaloid.

Remarks.—Hydrochloric acid is used in the initial menstruum to insure the complete extraction of the strychnine. Note that an alkaloidal assay (see Chap. LVI) is provided for this tincture and that the strength is estimated in terms of strychnine, the most important and active alkaloid of nux vomica. The U.S.P. X gave a total alkaloid standard and the assay was made for total alkaloids. In the U.S.P. XI assay, the strychnine is estimated separately.

Dose.—1 cc. (15 minims).

TINCTURA OPII—Tincture of Opium

(Tr. Opii—Laudanum, Tincture of Deodorized Opium, Tinctura Opii P.I.)

Tincture of Opium yields, from each 100 cc., not less than 0.95 Gm. and not more than 1.05 Gm. of anhydrous morphine.

Alcohol Content.—17 to 19 per cent by volume.

Condensed Recipe.

Upon 100 Gm. of granulated opium pour 500 cc. boiling water, stirring frequently during twenty-four hours. Percolate with water to exhaustion. The percolate is concentrated on a water bath to 400 cc., boiled actively for fifteen minutes and allowed to stand overnight. Heat to 80° C. and add 50 Gm. of paraffin, after which the mixture is warmed until the paraffin melts. The mixture is then beaten and after cooling the cake of paraffin is removed, the fluid is filtered and sufficient water to make 750 cc. is added. Now add 188 cc. of alcohol and assay. Dilute the liquid with a mixture of alcohol, 1 volume, and water, 4 volumes, as required to bring the tincture to the official standard. For details, see U.S.P., p. 404.

Remarks.—In the U.S.P. X, the old form of tincture of opium was dropped and the refined product, tincture of deodorized opium, was rechristened "Tinctura opii" and even given the synonym, "laudanum." The old tincture of opium was made by treatment of granulated opium with water and alcohol; the present tincture represents an evaporated aqueous percolate of opium deprived of its odor by beating up with melted paraffin and then mixing with enough alcohol to preserve it.

The old-style tincture of opium was known centuries ago under such names as *laudanum* and *tinctura thebaica.* Tincture of opium prepared by the recipe of U.S.P. X was introduced some sixty years ago as a proprietary and was formerly called *denarcotized tincture of opium,* since erroneously thought to be free from narcotine, to which the unpleasant after-effects of ordinary laudanum were supposedly due. A chemical assay process is given for this tincture which is described in detail in the U.S.P., pages 405 and 272.

TINCTURA OPII CAMPHORATA—Camphorated Tincture of Opium

(Tr. Opii Camph.—Paregoric, Tinctura opii benzoica P.I.)

Camphorated Tincture of Opium yields, from each 100 cc., not less than 0.035 Gm. and not more than 0.045 Gm. of anhydrous morphine.

Alcohol Content.—43 to 46 per cent by volume.

Condensed Recipe.

Dissolve 40 cc. Tincture of Opium; 4 Gm. benzoic acid; 4 Gm. camphor, and 4 cc. of oil of anise in diluted alcohol, 900 cc.; add 40 cc. glycerin and then sufficient diluted alcohol (U.S.P.) to make 1000 cc. Agitate the mixture and filter. For details, see U.S.P., p. 405.

Remarks.—This popular official is commonly called *paregoric,* the latter word meaning "soothing," the tincture being originally called "elixir paregoricus," soothing elixir. Note that it contains 0.4 of 1 per cent of opium and that it is a constituent of brown mixture (p. 279). A chemical assay process is given in the Pharmacopœia for this preparation based on the morphine content of the tincture of opium used in its manufacture.

Dose.—4 cc. (1 fluidrachm).

TINCTURA RHEI AROMATICA—Aromatic Tincture of Rhubarb

(Tr. Rhei Arom.)

Condensed Recipe.

Moisten 200 Gm. rhubarb, 40 Gm. cinnamon, 40 Gm. clove, and 20 Gm. nutmeg, each in a No. 40 powder, with the menstruum—alcohol, 500 cc.; water, 400 cc.; glycerin, 100 cc.; macerate and then percolate to 1000 cc., using diluted alcohol as the final menstruum. See details in U.S.P., p. 406.

Remarks.—Note the aromatic constituents of this tincture, which is rarely prescribed, and which is official chiefly because used in making the official aromatic syrup of rhubarb (p. 220).

Dose.—4 cc. (1 fluidrachm).

TINCTURA SCILLÆ—Tincture of Squill

(Tr. Scill.—Tinctura Scillæ P.I.)

Alcohol Content.—64 to 67 per cent by volume.

Condensed Recipe.

Squill (100 Gm.) in No. 40 powder, is moistened with the menstruum—alcohol, 3 volumes; water, 1 volume—macerated and percolated until 1000 cc. of tincture are obtained. For details, see U.S.P., p. 407.

Remarks.—In the U.S.P. X a biological assay was prescribed for this tincture similar to that for Tinctura Digitalis. The present Pharmacopœia requires no assay and does not provide a standard for the finished product.

Dose.—1 cc. (15 minims).

TINCTURA STRAMONII—Tincture of Stramonium

(Tr. Stramon.)

Tincture of Stramonium yields, from each 100 cc., not less than 0.027 Gm. and not more than 0.033 Gm. of the alkaloids of stramonium.

Alcohol Content.—64 to 70 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of the drug in a No. 40 powder with the menstruum—alcohol, 3 volumes; water, 1 volume; macerate and then percolate to 950 cc. Use the same menstruum for adjusting the finished product to the official alkaloidal standard. For details, see U.S.P., p. 407.

Remarks.—The Pharmacopœial assay for this tincture is a chemical assay based upon its content of stramonium alkaloids which are of the mydriatic variety.

Dose.—0.75 cc. (12 minims).

TINCTURA VALERIANÆ—Tincture of Valerian

(Tr. Valer.)

Alcohol Content.—66 to 70 per cent by volume.

Condensed Recipe.

Moisten 200 Gm. of the drug in a No. 40 powder with the menstruum—alcohol, 3 volumes; water, 1 volume; macerate and then percolate to 1000 cc. For details, see U.S.P., p. 408.

Dose.—4 cc. (1 fluidrachm).

TINCTURA VERATRI VIRIDIS—Tincture of Veratrum Viride

(Tr. Verat. Vir.)

Alcohol Content.—88 to 92 per cent by volume.

Condensed Recipe.

Moisten 100 Gm. of the drug in a No. 60 powder with the menstruum—alcohol (U.S.P.); macerate and then percolate to 1000 cc. For details, see U.S.P., p. 408.

Remarks.—While the U.S.P. VIII directed a tincture of veratrum made either from *Veratrum album* or from *Veratrum viride,* the U.S.P. X and XI recognize only the latter drug—green hellebore—and so the preparation now under consideration is a tincture of veratrum viride. It is a 10 per cent tincture; quite different from the tincture of the Pharmacopœia of 1890 which was a 40 per cent product. The latter closely simulated *Norwood's tincture of veratrum,* formerly largely prescribed.

Dose.—1 cc. (15 minims).

Tinctura Aloes (U.S.P. IX; N.F. VI) is made by macerating 100 Gm. aloe and 200 Gm. glycyrrhiza with enough diluted alcohol to make 1000 cc. *Dose.*—2 cc. (30 minims).

Tinctura Arnicæ (U.S.P. IX; N.F. VI) is a 20 per cent tincture prepared by interrupted percolation; that is, the percolation is stopped after 500 cc. of tincture have been collected in order to permit new portions of menstruum (diluted alcohol) to act by maceration upon the partly extracted drug. In the N.F. V percolation was interrupted three times. In U.S.P. VIII, fractional maceration followed by expression was employed—a wise provision since the drug is very bulky and highly absorbent; hence percolation means a large waste of menstruum, unless the marc is expressed. This tincture is used as a vulnerary. It is rarely used internally. *Dose.*—0.5 cc. (8 minims).

Tinctura Asafœtidæ (U.S.P. X; N.F. VI) or *Tincture of Asafetida* is prepared by macerating asafetida (200 Gm.) with alcohol for three days. The mixture is filtered and the filter washed with enough alcohol to make 1 liter. For details, see N.F. VI, p. 397. *Dose.*—1 cc. (15 minims).

Tinctura Calumbæ (U.S.P. X; N.F. VI) or *Tincture of Calumba* is made by moistening 200 Gm. drug in No. 20 powder with the menstruum of alcohol, 2 volumes; water, 1 volume—macerate and then percolate to 1000 cc. For details, see N.F., p. 399. *Dose.*—4 cc. (1 fluidrachm).

Tinctura Cannabis (U.S.P. IX; N.F. VI) is a 10 per cent tincture made by percolating the drug with alcohol. This preparation was not in the N.F. V. *Dose.*—1 cc. (15 minims).

Tinctura Cardamomi (U.S.P. X) or *Tincture of Cardamom* is prepared by moistening 200 Gm. of cardamom seed in No. 40 powder with diluted alcohol (U.S.P.); macerating and then percolating with the same menstruum to 1000 cc. Details as in making tincture of bitter orange peel. This is *plain* tincture of cardamom and not to be confused with the compound tincture so largely used as an aromatic and carminative. *Dose.*—2 cc. (30 minims).

Tinctura Cinchonæ (U.S.P. X) or *Tincture of Cinchona* is made of such strength that each 100 cc. contains 0.8 to 1 Gm. of cinchona alkaloids. It is prepared by percolating cinchona (200 Gm.) with a primal menstruum consisting of 75 cc. of glycerin, 675 cc. of alcohol and 250 cc. of water, completing the percolation with a mixture of 2 volumes of alcohol and 1 volume of water. Scoville prefers an acidulated menstruum in making this tincture (p. 269), but Lichtin believes it preferable to remove the tannin by a preliminary extraction of the bark with acetone and final percolation of the detannated bark with 78 per cent alcohol and 7.5 per cent of glycerin. *Dose.*—4 cc. (1 fluidrachm).

Tinctura Cinnamomi (U.S.P. IX; N.F. VI) is a 20 per cent tincture made by percolation with a menstruum consisting of alcohol, 3 volumes; water, 1 volume. After 925 cc. of percolate is collected, 75 cc. of glycerin are added. *Dose.*—2 cc. (30 minims).

Tinctura Gambir Composita (U.S.P. X; N.F. VI) or *Compound Tincture of Gambir*, also known as *Compound Tincture of Pale Catechu* is made by macerating 200 Gm. of gambir in a No. 40 powder and 100 Gm. cinnamon in a No. 60 powder, with a menstruum of alcohol, 9 volumes; glycerin, 1 volume, to make 1000 cc. tincture. This tincture is four times the strength of the U.S.P. X product and replaces the formerly official *tincture of catechu.* Pale catechu (gambir), is used instead of the catechu from the plant *Acacia catechu.* (See p. 812.) *Dose.*—2 cc. (30 minims).

Tinctura Gelsemii (U.S.P. IX; N.F. VI) is a 10 per cent tincture made by percolation with a menstruum consisting of 4 volumes of alcohol and 1 volume of water. *Dose.*—0.3 cc. (5 minims).

Tinctura Guaiaci (U.S.P. IX; N.F. VI) is a 20 per cent tincture made by maceration with alcohol. *Dose.*—4 cc. (1 fluidrachm).

Tinctura Guaiaci Ammoniata (U.S.P. IX; N.F. VI) is a 20 per cent tincture of guaiac made by macerating the drug with aromatic spirit of ammonia. *Dose.*—2 cc. (30 minims).

Tinctura Hydrastis (U.S.P. IX; N.F. VI) is a 20 per cent tincture made by percolating the drug with a mixture of 2 volumes of alcohol and 1 volume of water. It is to be assayed and adjusted to the strength of not less than 0.45 Gm. and not more than 0.55 Gm. of ether-soluble alkaloids of hydrastis. *Dose.*—8 cc. (2 fluidrachms).

Tinctura Ipecacuanhæ et Opii (U.S.P. VIII; N.F. VI) is commonly known as *tincture of Dover's powder.* It is made by evaporating 1000 cc. of tincture of opium to a volume of 580 cc.; in order that 100 cc. of fluidextract of ipecac may be added along with enough diluted alcohol to bring the total volume to 1 liter. Thus the finished preparation represents 10 per cent of opium and 10 per cent of ipecac.

Tinctura Krameriæ (U.S.P. X) or *Tincture of Krameria* is made by moistening 200 Gm. of the drug in a No. 40 powder with the menstruum—diluted alcohol U.S.P.; then macerating and percolating to 1000 cc. Details as in making tincture of bitter orange peel. This is the only tincture admitted to U.S.P. X that was not in U.S.P. IX. It was official in U.S.P. VIII. It has again been discarded and is not listed in the N.F. *Dose.*—4 cc. (1 fluidrachm).

Tinctura Lactucarii (U.S.P. IX) is essentially a 50 per cent tincture made by percolating with a menstruum consisting of glycerin, 250 cc.; water, 250 cc.; and alcohol, 500 cc. Its method of preparation is interesting in that the lactucarium is first washed with petroleum benzin to remove the rubber-like, inert substance it contains. The benzin used must be of pharmacopœial purity, as commercial benzin is too impure for pharmaceutical purposes. (See p. 642.) The drug is not easily exhausted with the menstruum employed, and in making 1000 cc., the first 750 cc. of percolate is reserved and the rest of the percolate evaporated, similar to making fluidextracts. *Dose.*—2 cc. (30 minims).

Tinctura Lobeliæ (U.S.P. X; N.F. VI) or *Tincture of Lobelia* is made by macerating 100 Gm. of the drug in a No. 40 powder with the menstruum—diluted alcohol (U.S.P.), 995 cc. and acetic acid, 5 cc., and then percolating. The percolation is completed with diluted alcohol (U.S.P.). *Dose.*—1 cc. (15 minims).

Tinctura Moschi (U.S.P. IX) is a 5 per cent tincture made by maceration with a menstruum that is essentially diluted alcohol. The manipulation however is somewhat intricate, the tincture being made by rubbing musk with water, adding alcohol, filtering, and washing residue with diluted alcohol.

It should be prepared with the utmost care, for when it is required, a fine quality is absolutely essential, it being used chiefly as a stimulant in extreme cases of pneumonia. *Dose.*—4 cc. (1 fluidrachm).

Tinctura Physostigmatis (U.S.P. IX) is a 10 per cent tincture made by percolation with alcohol. U.S.P. IX directed it to be assayed and adjusted to the basis of $^{15}/_{1000}$ of 1 per cent of physostigma alkaloids. *Dose.*—1 cc. (15 minims).

Tinctura Pyrethri (U.S.P. IX) is a 20 per cent tincture made by percolation with alcohol. As this rarely used tincture was employed almost entirely externally (as a toothache remedy) no dose was given for it in U.S.P. IX.

Tinctura Quassiæ (U.S.P. IX; N.F. VI) is a 20 per cent tincture made by percolating the drug with a mixture of 1 volume of alcohol and 2 volumes of water. *Dose.*—2 cc. (30 minims).

Tinctura Quillajæ (U.S.P. VIII; N.F. VI) also called Tincture of Soap Bark is an aqueous decoction of soap bark with enough alcohol (350 cc. to the liter) added to preserve it. The preparation is used as an emulsifying agent (see p. 282), but it should never be used for that purpose except under direct orders of a physician, since the saponin of the bark is distinctly poisonous. It is used as a "gum foam" at the soda fountain, and this use is also objectionable and is prohibited in some states.

Tinctura Rhei Composita (U.S.P. X; N.F. VI) or *Compound Tincture of Rhubarb*, listed as *Tincture of Rhubarb* in the U.S.P. X., is made by moistening 200 Gm. rhubarb and 30 Gm. cardamom seed, each in a No. 40 powder with the menstruum—alcohol, 500 cc.; water, 400 cc.; glycerin, 100 cc.; macerating and then percolating to 1000 cc., using diluted alcohol as the final menstruum. Note that this tincture contains cardamom seed besides rhubarb; one of the few cases where a preparation containing more than one drug was not pharmacopœially termed "compound." However the National Formulary now lists this tincture under the name of "Compound Tincture of Rhubarb." *Dose.*—4 cc. (1 fluidrachm).

Tinctura Sanguinariæ (U.S.P. IX; N.F. VI) is a 10 per cent tincture made by percolation. It is one of the few U.S.P. and N.F. tinctures extracted with menstruum containing acid, and it is worth noting that 1000 cc. of finished tincture contains but 10 cc. of hydrochloric acid; that all this is mixed with the menstruum used in moistening the drug; and that all the menstruum used in percolation is hydro-alcoholic. *Dose.*—1 cc. (15 minims).

Tinctura Strophanthi (U.S.P. X; N.F. VI) or *Tincture of Strophanthus* (Strophanthi tinctura P.I.) is made by freeing 100 Gm. of strophanthus from fat by percolating with purified petroleum benzin, drying and then moistening with alcohol, macerating forty-eight hours and then percolating with alcohol until 950 cc. of tincture is obtained. Following the assay the strength is adjusted by using more of the same menstruum in proper proportion. For details, see N.F., p. 414. A biological assay is prescribed using the frog as test animal. *Dose.*—0.5 cc. (8 minims).

Tinctura Valerianæ Ammoniata (U.S.P. X; N.F. VI) or *Ammoniated Tincture of Valerian* is made in the same manner as tincture of valerian, but aromatic spirit of ammonia is employed as the menstruum. Note that this and the N.F. ammoniated tincture of guaiac are the only official tinctures made with aromatic spirit of ammonia. *Dose.*—2 cc. (30 minims).

Tinctura Vanillæ (U.S.P. VIII; N.F. VI) is made by macerating cut vanilla beans with water for twelve hours and then in adding alcohol and continuing the maceration for three days. The mixture is transferred to a percolator containing 200 Gm. of sucrose and drained. The drug is then packed and percolated with diluted alcohol (U.S.P.). The resulting product represents 10 per cent of vanilla beans and contains 20 per cent of sucrose in what is approximately diluted alcohol and is a fine grade of the flavoring *essence of vanilla.* What is commonly sold under this name, however, is a concoction of various inferior flavors, such as coumarin and possibly some vanillin. Another point in connection with the manufacture of the tincture of vanilla is that, in order to secure a really fine tincture of vanilla, it is essential to use a good quality of vanilla bean. The inferior Tahiti beans can never yield anything but a poor product. To preserve the aroma of the tincture it should be stored in glass containers.

Tinctura Zingiberis (U.S.P. X) or *Tincture of Ginger* is made by moistening 200 Gm. of the drug in a No. 40 powder with the menstruum—alcohol, 850 cc.; water, 150 cc.; macerating and then percolating to 1000 cc. Details as in making tincture of bitter orange peel. This is the well-known *essence of ginger.* It represents 20 per cent of the drug, and is made with approximately 80 per cent alcohol: Beringer and Randolph finding that menstruum sufficiently strong for preparing a 20 per cent tincture. When mixed with water, it forms a milky mixture, due to the separation of the resin. The so-called "water-soluble ginger" is the tincture rubbed with magnesium carbonate and enough water to precipitate much of the resin. The U.S.P. X gave an "organoleptic" test for the presence of capsicum as this drug has been used as an adulterant for ginger. It is important to note that this 20 per cent essence of ginger can no longer be sold over the counter; the alcohol-regulatory authorities having declared it "an intoxicating beverage." The same ruling classed as unfit for beverage purposes a 40 per cent essence of ginger. During 1929 and 1930 illegal essence of ginger containing poisonous

TINCTURES OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Tinctura aloes.			See p. 252.
Tinctura aloes et myrrhæ.	Tincture of aloe and myrrh.	Aloe, myrrh and glycyrrhiza of each 100 Gm. Menstruum, alcohol, 750 cc.; water, 250 cc.	Made by maceration, Was official in U.S.P. VIII. *Dose.*—2 cc. (30 minims).
Tinctura antimonii.	Tincture of antimony.	Tartar emetic, 4 Gm., distilled water; caramel; acetic ether; alcohol, 200 cc.	Replacing *wine of antimony*, N.F. IV (p. 245). *Dose.*—1 cc. (15 minims).
Tinctura arnicæ.			See p. 252.
Tinctura asafœtidæ.	Tincture of asafetida.	Asafetida, 200 Gm.; alcohol as menstruum.	*Dose.*—1 cc. (15 minims).
Tinctura bryoniæ.	Tincture of bryonia.	Bryonia, 200 Gm.; alcohol.	Made by percolation *Dose.*—4 cc. (1 fluidrachm).
Tinctura cacti grandiflori.	Tincture of night blooming cereus.	Cactus grandiflorus, 500 Gm.; alcohol.	Made by maceration of the fresh flowers with subsequent expression. *Dose.*—1 cc. (15 minims).
Tinctura calendulæ.	Tincture of marigold.	Calendula, 200 Gm ; alcohol.	Made by percolation. Was official in U.S.P. VIII. *Dose.*—4 cc. (1 fluidrachm).
Tinctura calumbæ.	Tincture of calumba.	Calumba. Menstruum, alcohol, 2 volumes, water, 1 volume.	*Dose*—4 cc. (1 fluidrachm).
Tinctura cannabis.	Tincture of cannabis.	Cannabis, 100 Gm.; alcohol.	*Dose*—1 cc. (15 minims).
Tinctura capsici et myrrhæ.	Hot drops, number six.	Capsicum, 30 Gm ; myrrh, 120 Gm. Menstruum, alcohol, 9 volumes; water, 1 volume.	Made by percolation of the drugs mixed with sand. *Dose.*—2 cc. (30 minims).
Tinctura cimicifugæ.	Tincture of cimicifuga.	Cimicifuga, 200 Gm.; alcohol.	Made by percolation. Was official in U.S.P. VIII. *Dose.*—4 cc.; (1 fluidrachm).
Tinctura cinnamomi.			See p. 252.
Tinctura cocculi.	Tincture of fish berries.	Cocculus, 100 Gm.; diluted alcohol	Made by percolation. Used as vermin killer.
Tinctura colchici cormi fortis.	Strong tincture of colchicum corm	Fluidextract of colchicum corm, 400 cc.; alcohol, 1 volume; water, 3 volumes.	Replacing *wine of colchicum corm* N.F. IV. *Dose.*—0.6 cc. (10 minims).
Tinctura cubebæ.	Tincture of cubeb	Cubeb, 200 Gm.; alcohol, 9 volumes; water, 1 volume.	Made by percolation. *Dose*—8 cc. (2 fluidrachms).
Tinctura delphinii.	Tincture of larkspur.	Larkspur seed, 100 Gm ; alcohol.	Made by percolation. Used as vermin killer.
Tinctura delphinii acetica.	Acetic tincture of larkspur.	Larkspur; acetic acid; alcohol; glycerin; water.	Used as a parasiticide.
Tinctura ferri citrochloridi.	Tasteless tincture of iron.	Solution of ferric chloride, 350 cc.; sodium citrate, 450 Gm.; alcohol; water.	See p. 567. *Dose.*—0.5 cc. (8 minims).
Tinctura gallæ.	Tincture of nutgall.	Nutgall, 200 Gm. Menstruum, glycerin, 100 cc.; alcohol, 900 cc.	Replaces the tincture of U.S.P. VIII. *Dose.*—4 cc. (1 fluidrachm).
Tinctura gambir composita.	Compound tincture of gambir.	Gambir; cinnamon; glycerin; alcohol.	*Dose.*—2 cc. (30 minims).
Tinctura gelsemii.			See p. 253.
Tinctura guaiaci.			See p. 253.

TINCTURES OF THE NATIONAL FORMULARY—(*Continued*)

Latin name.	English name or synonym.	Ingredients (figures show amount used in 1000 cc.).	Remarks.
Tinctura guaiaci ammoniata.			See p. 253.
Tinctura hydrastis.			See p. 253.
Tinctura iodidorum.	Decolorized tincture of iodine.	Iodine, 50 Gm.; potassium iodide; stronger ammonia water, 100 cc.; water, alcohol.	Replaces the recipe of N.F. IV. See p 427.
Tinctura iodi fortior.	Churchill's tincture of iodine.	Iodine, 165 Gm.; potassium iodide, 35 Gm ; water, alcohol.	Over twice as strong as the U.S.P. tincture.
Tinctura ipecacuanhae.	Tincture of ipecac.	Fluidextract of ipecac, 100 cc.; diluted hydrochloric acid; alcohol; distilled water.	Made by simple solution. Replaces *wine of ipecac*, N.F. IV *Dose.*—0.6 cc. (10 minims).
Tinctura ipecacuanhæ et opii.	Tincture of Dover's powder.		See p. 253.
Tinctura jalapæ.	Tincture of jalap.	Jalap, 200 Gm. Menstruum, alcohol, 9 volumes; water, 1 volume.	Made by percolation. *Dose*—4 cc. (1 fluidrachm).
Tinctura lobeliæ.	Tinctura of lobelia.	Lobelia, 100 Gm.; acetic acid; diluted alcohol.	*Dose.*—1 cc. (15 minims).
Tinctura persionis.	Tincture of cudbear.	Cudbear, 100 Gm Menstruum, alcohol, 3 volumes; water, 1 volume.	Made by percolation Used as a coloring agent.
Tinctura persionis composita.	Compound tincture of cudbear.	Tincture of cudbear, 150 cc.; caramel, 100 Gm.; alcohol; water.	Made by admixture Used as a coloring agent.
Tinctura pulsatillæ.	Tincture of pulsatilla.	Pulsatilla, 100 Gm. Menstruum, alcohol, 3 volumes; water, 1 volume.	Made by percolation. *Dose.*—2 cc. (30 minims).
Tinctura quassiæ.			See p. 254.
Tinctura quillajæ.	Tincture of soap bark.		See p 254.
Tinctura rhei composita.	Compound tincture of rhubarb; tincture of rhubarb.	Rhubarb; cardamom seed; glycerin Menstruum, glycerin, alcohol and water; followed by diluted alcohol.	*Dose.*—4 cc. (1 fluidrachm).
Tinctura rhei dulcis.	Sweet tincture of rhubarb.	Rhubarb, 100 Gm ; glycyrrhiza; anise; cardamom seed. Menstruum, glycerin, alcohol and water; followed by diluted alcohol.	Made by percolation *Dose.*—4 cc. (1 fluidrachm).
Tinctura sanguinariæ.			See p. 254.
Tinctura serpentariæ.	Tincture of serpentaria.	Serpentaria, 200 Gm. Menstruum, alcohol, 4 volumes; water, 1 volume	Made by percolation Was official in U.S. P VIII *Dose.*—4 cc. (1 fluidrachm).
Tinctura strophanthi.	Tincture of strophanthus.	Strophanthus, 100 Gm. Purified petroleum benzine to defat the drug. Alcohol as menstruum	*Dose.*—0.5 cc. (8 minims).
Tinctura valerianæ ammoniata.	Ammoniated tincture of valerian.	Valerian, 200 Gm. Aromatic spirit of ammonia as menstruum.	*Dose*—2 cc. (30 minims).
Tinctura vanillæ.	Tincture of vanilla.		See p. 254.
Tinctura viburni opuli composita.	Compound tincture of viburnum.	Viburnum opulus; dioscorea; scutellaria; clove; cinnamon. Menstruum, glycerin, alcohol, water; then alcohol, 3 volumes; water, 1 volume.	Made by percolation. *Dose.*—4 cc. (1 fluidrachm).
Tincturæ ætheræ.	Ethereal tinctures.		See p. 257.
Tincturæ medicamentorum recentium.	Tinctures of fresh drugs.		See p. 257.

tri-ortho-tolyl-phosphate produced havoc in certain sections of this country, causing paralysis and death in some cases. Since ginger preparations have been so grossly misused under the guise of medicinal products, the tincture has been eliminated from both U.S.P. and N.F. *Dose.*—2 cc. (30 minims).

Tincturæ Æthereæ (N.F.) represent a class of tinctures in which the menstruum employed consists of alcohol and ether. The National Formulary gives a general formula for such preparations directing that the menstruum consist of 1 volume of ether and 2 volumes of alcohol and that the finished tincture represents 10 per cent of the drug used. Ethereal tincture of valerian enjoys some vogue.

Tincturæ Medicamentorum Recentium (U.S.P. VIII; N.F. VI) or *Tincturæ Herbarum Recentium*, Tinctures of Fresh Herbs, are a line of preparations made by macerating 500 Gm. of the fresh herb or drug for fourteen days with alcohol after which the mixture is expressed; the expressed liquid strained and enough alcohol is added to make 1 liter. They resemble the *juices* (Succi) of the British Pharmacopœia and are rarely used in this country.

THE DOSES OF OFFICIAL TINCTURES

0.1 cc. (1½ minims)........	Tinctures of cantharides and iodine.
0.3 cc. (5 minims)...........	Tincture of gelsemium (N.F. VI).
0.5 cc. (8 minims)...........	Tinctures of capsicum, ferric citrochloride (N.F. VI), ipecac and opium (N.F. VI) and strophanthus (N.F. VI).
0.6 cc. (10 minims)..........	Tinctures of aconite, belladonna, colchicum corm, strong (N.F. VI), ferric chloride, ipecac (N.F. VI), and opium.
0.75 cc. (12 minims).........	Tincture of stramonium.
1 cc. (15 minims)...........	Tinctures of antimony (N.F. VI), arnica (N.F. VI), asafetida (N.F. VI), benzoin, cactus grandiflorus (N.F. VI), cannabis (N.F. VI), cinnamon (N.F. VI), digitalis, lobelia (N.F. VI), nux vomica, sanguinaria (N.F. VI), squill and veratrum viride.
2 cc. (30 minims)...........	Tinctures of aloe (N.F. VI), aloe and myrrh (N.F. VI), benzoin compound, capsicum and myrrh (N.F. VI), colchicum seed, gambir compound (N.F. VI), guaiac ammoniated (N.F. VI), hyoscyamus, kino, lavender compound, myrrh, pulsatilla (N.F. VI), quassia (N.F. VI), tolu balsam and valerian ammoniated (N.F. VI).
4 cc. (1 fluidrachm).........	Tinctures of bitter orange peel, bryonia (N.F. VI), calendula (N.F. VI), calumba (N.F. VI), cardamom compound, cinchona compound, cimicifuga (N.F. VI), gentian compound, guaiac (N.F. VI), jalap (N.F. VI), nutgall (N.F. VI), opium camphorated, rhubarb aromatic, rhubarb compound (N.F. VI), rhubarb sweet (N.F. VI), serpentaria (N.F. VI), sweet orange peel, valerian and viburnum compound (N.F. VI).
8 cc. (2 fluidrachms).........	Tinctures of cubeb (N.F. VI) and hydrastis (N.F. VI).
No doses given.............	Tinctures of cudbear (N.F. VI), cudbear compound (N.F. VI), cocculus (N.F. VI), iodine mild, iodine stronger, iodides (N.F. VI), larkspur (N.F. VI), larkspur acetic (N.F. VI), lemon, quillaja, and vanilla.

FLAVORING EXTRACTS

These are preparations used to impart flavors to food and drink. Sometimes they are called "extracts" and sometimes "essences." A number of them are pharmaceutical spirits, such as the spirits of lemon, of peppermint and of orange described on the preceding pages. As a rule however, the medicinal spirits such as spirit of peppermint are much stronger than the flavoring essences. In the case of peppermint the medicinal product is 10 per cent, whereas the usual flavoring essence is about 5 per cent. "Extract of almond" on the other hand should be made from an oil of almond that has been freed from its hydrocyanic acid (see p. 793). Other of the flavoring extracts are pharmaceutical tinctures. Thus for "extract of vanilla," tincture of vanilla N.F. should be employed. The old-fashioned "essence of ginger" (tincture of ginger, U.S.P.) representing a 20 per cent tincture is now taboo, the national alcohol-regulatory authorities declaring it to be an intoxicating beverage (p. 254).

Other so-called "extracts" are blends of certain esters such as butyric ether, acetic ether and amyl acetate with alcohol and water. In some cases other aromatics (such as orris) are added and appropriate colors are employed. Most of the recipes for these factitious "extracts" are based on those proposed by Kletzinsky (1866) but recently Power and Chestnut have attacked the subject in a scientific manner distilling large quantities of apple parings and pulp and peach pulp and studying the oils obtained. Their work shows that the flavor of the peach consists of the linalyl esters of formic, acetic, valeric and caprylic acids with a considerable portion of acetaldehyde while the flavor of the apple consists of the iso-amyl esters of formic, acetic, caproic and caprylic acids, acetic acid, geraniol,. geranyl formate and geranyl acetate. The aroma of the grape is largely due to esters of anthranilic acid.

During the period of prohibition, the status of some of these essences, notably ginger and vanilla was questioned and *alcohol-free* extracts have been discussed. These consist of the flavors (*a*) mixed with syrup or glucose (*b*) dissolved in oils (*c*) mixed with glycerin or (*d*) emulsified with gum and water.

BIBLIOGRAPHY

Infusions.—(Manufacture) Alsop, A.J.P., 8, 1836, 89; Bell, Jl. 1, 1841, 54; Rice, Am. Dr., 14, 1885, 45; Martindale, Ph. Jl. [4], 1, 1895, 415. (Infusion of digitalis) Hatcher and Eggleston, Jl. A.M.A., 65, 1915, 1902; Pomeroy and Heyl, A.J.P., 92, 1920, 394; Hatcher and Weiss, Jl. A.Ph.A., 10, 1921, 441; Bliss, *ibid.*, 10, 1921, 757; Anon., A.J.P., 97, 1925, 456; Tainter, Jl. A.Ph.A., 15, 1926, 255; Cloetta, Arch. exp. Path. u. Pharmakol., 112, 1926, 261; Hintzelmann and Joachimoglu, Jl. Soc. Ch. Ind., 45, 1926, 607 B; Otto, Dr. Circ., 73, 1929, 472; Hatcher and Haag, Jl. A.Ph.A., 18, 1929, 551 and 670; Wokes and Elphich, Quart. J. Pharm., 3, 1930, 73; Hoekstra and ten Kleij, C. A., 26, 1932, 2276. (Infusion of ipecac) Bauer and Heber, Ph. Cent., 71, 1930, 513. (Black draught *vs.* black drop) Wiley, Pharmacal Jurisprudence, 1889, 233.

Decoctions.—(Manufacture) Powers, A.J.P., 5, 1834, 104. (Zittmann's) Anon., A.J.P., 7, 1835, 175; Saunders, A.Ph.A., 15, 1867, 339.

Tinctures.—(Manufacture) Lloyd, Ph. Rev., 21, 1903, 25. Simon, Ph. Jl., 107, 1921, 519. (Made from fluidextracts) Davy, Jl. A.Ph.A., 8, 1919, 112; Scoville, Jl. A.Ph.A., 4, 1915, 1472. (Keeping) Kunz-Krause, Spatula, 11, 1905, 679; Scoville, Jl. A.Ph.A., 16, 1927, 1136. (Aconite) Swanson, Jl. A.Ph.A., 13, 1924, 1108. (Friar's balsam) Wootton, 2, 1910, 135. X-rayser II, Ch. and Dr., 89, 1917, 155; Peacock, Jl. A.Ph.A., 8, 1919, 482; Cocking, Ph. Jl., 121, 1928, 86. (Cantharides) Nitardy, Jl. A.Ph.A., 12, 1923, 142. Scoville, *ibid.*, 9, 1920, 864 and 10, 1921, 844. (Capsicum) Poe, Wyss and Slator, Jl. A.Ph.A., 19, 1930, 1188. (Cardamom, compound) Abraham and Rae, Ph. Jl., 126, 1931, 399. (Cinchona) Scoville, Jl. A.Ph.A., 9, 1920, 864 and 10, 1921, 844; Lichtin, A.J.P., 102, 1930, 583 and 103, 1931, 279. (Digitalis) England, A.Ph.A., 48, 1900, 530; Hatcher and Eggleston, Year Book, A.Ph.A., 2, 1913, 501; Krantz, Jl. A.Ph.A., 19, 1930, 366 and 22, 1933, 106. (Ginger) Randolph and Beringer, Jl. A.Ph.A., 13, 1924, 27; Anon, Regulations, 60, Sec. 811, Gov't. Printing Office, Washington, 1924, 83; Eden, Marsh and Lythgoe, Jl. Ind. Eng. Ch., 16, 1924, 816, (Toxic ginger) Smith, Elvove and Frazier, C. A., 25, 1931, 348; Valaer, A.J.P., 102, 1930, 571. (Huxham's tincture) Wootton, 2, 1910, 67 and 100. (Kino) White, Ph. Jl., 70, 1903, 644 and 71, 1903, 702. (Laudanum) Dodd, A.Ph.A., 46, 1898, 743; X-rayser, Ch. and Dr., 85, 1914, 723; Husemann, Arch. de. Pharm., 277, 1889, 1075 and 1105; Anon, Ph. Jl., 126, 1931; 222. (Paregoric) Wootton, 2, 1910, 193, 151. Sargent, Spatula, 20, 1914, 211 and 271. (Opium, denarcotized) Rother, A.J.P., 55, 1883, 76 and 598; Ebert, A.J.P., 39, 1867, 193 and 74, 1902, 157; Hodgson, Merck's Rep., 11, 1902, 462. (Nux vomica) Thum. Jl. A.Ph.A., 9, 1920, 704. (Quillaga) Karsmark and Kofler, Arch. d. Pharm., 267, 1929, 424. (Vanilla) Schlotterbeck and Dean, Jl. Ind. Eng. Ch., 8, 1916, 607 and 703; Bartlett, Jl. A.Ph.A., 9, 1920, 706; Mange and Ehler, Jl. Ind. Eng. Ch., 16, 1924, 1258; Gnadinger, *ibid.*, 17, 1925, 303; Wilson and Sale, *ibid.*, 18, 1926, 283; Hollingshead and Otterbacher, *ibid.*, 18, 1926, 871; Smith, *ibid.*, 20, 1928, 1307; Kessler, C. A., 24, 1930, 3289. (Churchill's tincture of iodine) Raubenheimer, A.J.P., 91, 1919, 37. (Sydenham's laudanum) Mouchon, Jl. de. ph., 20, 1834, 397; Angeletti, C. A. 22, 1928, 4719.

Flavoring Extracts.—(General) Kletzinski, Dingler's Poly. Jl., through Pharm. J. [2] 8, 1867, 467; also U.S.D., 13th Ed., 1871, 1597; Graham, A.Ph.A., 55, 1907, 895. (Flavor of apple) Power and Chestnut, Jl. Am. Ch. Soc., 42, 1920, 1509 and *ibid.*, 44, 1922, 2938. (Flavor of peach) Power and Chestnut, *ibid.*, 43, 1921, 1725. (Flavor of grape) Sale and Wilson C. A., 20, 1926, 3519.

Nonalcoholic Flavoring Extracts.—Thurston, Mid. Dr. through Year Book, A.Ph.A., 8, 1919, 88; Boyles, Dr. Circ., 63, 1919, 525; De Groote, Am. Perf. through C.A., 14, 1920, 2039 and 3114; Year Book A.Ph.A., 10, 1921, 70; Foulser, *ibid.*, 10, 1921, 70; Schuette and Domogalla, Jl. Ind. Eng. Ch., 18, 1926, 1254.

CHAPTER XV

FLUIDEXTRACTS, WINES, OLEORESINS, AND VINEGARS

FLUIDEXTRACTS

FLUIDEXTRACTS are alcoholic liquid preparations made by percolation, representing in each cubic centimeter the activity of 1 Gm. of drug; in other words, they are 100 per cent tinctures.

The fluidextracts of the present Pharmacopœia, of the strength of 1 Gm. to the cubic centimeter, are 5 per cent weaker than those directed by the Pharmacopœia of 1870, which represented a troy ounce of drug to the fluidounce. The difference in these strengths is apparent when we appreciate the fact that while 1 cc. of water weighs a gram, a fluidounce of water weighs 454.6 grains and not 480 grains or 1 troy ounce.

Fluidextracts can be considered in the light of concentrated tinctures, and many official drugs have both the tincture and the fluidextract recognized by the Pharmacopœia. The advantages which the fluidextracts possess over tinctures and other preparations are: 1. That they possess a definite strength of 100 per cent, the same as that of the product from which derived. In that way the physician, knowing the dose of the drug, has no difficulty in knowing the dose of a fluidextract. 2. Fluidextracts are concentrated, a very small quantity of fluidextract sufficing, where a much larger quantity, sometimes ten times the amount, of a tincture will be needed. 3. Fluidextracts are permanent. Being made with alcoholic menstrua, they keep perfectly, and, in fact, frequently become better as they age.

History.—The first reference to fluidextracts that has been found in is a paper by Ellis (1835) in which it is stated that they "are preparations that have been popular in England within a few years past." The United States Pharmacopœia of 1850 recognized seven so-called "fluidextracts" and of these but one was a fluidextract in the modern sense of the term. Of the others, four were concentrated syrups and two were oleoresins. In the Pharmacopœia of 1860 twenty-five fluidextracts were recognized, and of these, fifteen were fluidextracts in the modern sense of the term.

Manufacture of Fluidextracts.—Five general processes have been suggested for the manufacture of fluidextracts: (*a*) percolation with partial evaporation; (*b*) fractional or divided percolation; (*c*) repercolation; (*d*) percolation with incomplete exhaustion; (*e*) maceration with hydraulic pressure. In addition, in special cases, the fluidextract is made by making an infusion or decoction of the drug and adding to this enough alcohol to keep the preparation from spoiling. The first, second, and sixth method are described at some length in the general formula for fluidextracts printed in the present Pharmacopœia and National Formulary. (See U.S.P., pp. 165 to 168 and N.F., pp. 153 to 156.)

Type Processes A and B, given in the pharmacopœial general formula, are both methods of percolation with partial evaporation, the only difference being whether the menstruum contains other components such as an acid or glycerin or not. In Process A, the drug is moistened with the required quantity of menstruum and macerated first outside then within the percolator for a certain length of time, and then percolated with the menstruum until exhausted. The period of moistening outside the percolator has been reduced from six hours in the U.S.P. X to fifteen minutes in the present Pharmacopœia.

It is practically impossible, by the ordinary process of percolation, to exhaust 100 Gm. of drug with the first 100 cc. of percolate; in most cases 100 Gm. are not exhausted until about 500 cc. of percolate have been obtained. Accordingly, in making fluidextracts we percolate the drug until it is exhausted, and instead of evaporating the entire percolate down to 100 cc., we reserve the first 85 cc. of percolate, subjecting to the heat of evaporation only the balance of percolate.

The first portion of the percolate is put to one side and labeled "reserved portion." The rest of the percolate, called "weak percolate," is then placed in an appropriate distilling apparatus in order to recover the alcohol, and when the alcohol is distilled, the residue is evaporated to a soft extract on a water bath. This soft extract is then dissolved in the reserved portion, and enough menstruum is added to bring the fluidextract up to the number of cubic centimeters equal to the number of grams of the drug with which we started. Of the details of this process two salient points need be mentioned. It will be noticed that we spare the first 85 per cent of percolate from the heat to which we subject the remainder of the percolate. This is because it is supposed that this 85 per cent of percolate contains the active principles of at least 85 per cent of the drug, and since it is without question that even the heat of the water bath may possibly modify some of the delicate constituents of the drug, it has been deemed advisable to expose the smallest possible quantity of the soluble part of the drug to such temperature. A second point is that we evaporate the weak percolate to a soft extract instead of merely to a point where it, plus the reserve portion, would measure the number of cubic centimeters of fluid equal to the number of grams of drug with which we started out. The reason for this is because the liquid part of such a residue consists wholly of water, and that there would be danger that adding the liquid to the reserve portion would cause a precipitation of some of the constituents of the reserved portion.

This process is not a satisfactory one either for the manufacturer or for the retailer. For the retailer, it is a tedious operation, requiring a large amount of time for evaporation of the reserve portion, and especially when the menstruum is a diluted alcohol. The second disadvantage of the process is the use of heat, which tends to dissociate some of the plant principles.

It will be noticed that the general formula specifies that in evaporation, the weak percolate must not be heated above 60° C. As the formula directs that the alcohol be "recovered" it is assumed that distillation be employed and this operation can occur at 60° C., only when carried on in a vacuum pan; a piece of apparatus that is too expensive to be used by the retail pharmacist.

In *Type Process B*, the menstruum from which the reserved portion is to be prepared contains glycerin or acid, while that which is used to exhaust the drug is to be free from these substances. The reason for this provision is to prevent the portion which must be evaporated from possible decomposition or from adding to the finished fluidextract an undue amount of either glycerin or acid which would not volatilize along with the alcohol and water. In the case of fluidextracts which must be adjusted to a definite alkaloidal standard, a portion of the reserved percolate in which the evaporated second percolate has been dissolved is assayed and the necessary adjustment in volume is made.

Type Process C of the Pharmacopœia also known as fractional or divided percolation is devised to permit the preparation of a fluidextract by percolation without evaporation. It is a modification of the well-known method of repercolation and will be explained with the latter below.

Type Process D directs the preparation of an infusion or decoction of the drug and the addition to it, when sufficiently concentrated, of enough alcohol to preserve it. The process is employed in making the official fluidextracts of cascara sagrada; cascara sagrada, aromatic; and glycyrrhiza.

Repercolation is a process devised by Dr. E. R. Squibb as a means of doing away with the use of heat in the preparation of fluidextracts. The manipulation can be expressed as follows:

Suppose we want to make 1000 cc. fluidextract of gentian; we take 1000 Gm. drug, and the first thing we do with it is to divide it into four portions of 250 Gm. each. The first 250 Gm. we moisten with the menstruum, pack, macerate, and percolate, just as in the regular official process, with the sole exception that the percolate, as it drops, is collected into several portions; the first 200 cc.—dark, heavy, and concentrated—being set aside as finished fluidextract, and the next portions of 250 cc. each put into bottles and labeled respectively "weak percolate No. 1," "weak percolate No. 2," "weak percolate No. 3," and so on until exhaustion. The writer's personal experience showed that, on an average, 250 Gm. drug is not completely exhuasted until 1250 to 1500 cc. of percolate have dropped, and it was his rule to use a 500-cc. bottle for weak percolate No. 4, and to let the last percolate drop therein until the drug was completely exhausted.

As the result of our first percolation we have, from 250 Gm. gentian:

Fluidextract	200 cc.
Weak percolate No. 1	250 cc.
Weak percolate No. 2	250 cc.
Weak percolate No. 3	250 cc.
Weak percolate No. 4 (say)	350 cc.

The first 200 cc. called "fluidextract" above is supposed to contain the active principles of 200 Gm. drug, the remaining active principles of the drug will be found in the 1100 cc. of weak percolates Nos. 1, 2, 3, and 4 and chiefly in percolates Nos. 1 and 2. Now we are ready to begin with the second batch of 250 Gm. of ground gentian. We moisten it, not with official menstruum, but with weak percolate No. 1 of the previous operation. Then we pack and macerate, then pour in weak percolate No. 2, and after it has soaked in, we pour on weak percolate No. 3, and as that too sinks down as the liquid drops below, we pour on weak percolate No. 4. When that has gone through, we begin to employ the official menstruum. In the meanwhile the liquid dropping from the percolator has been collected in several portions. The first 250 cc. has been set aside as finished fluidextract. Note that this time we do not set aside the first 200 cc. as finished fluidextract, as we did in the previous case, but 250 cc.; for we began percolation this time, not with official menstruum, but with those percolates from the first batch of drug, containing the active principles of about 50 Gm. of said drug. The first 250 cc. from the second batch of drug was assumed to contain the active principles of 250 Gm. of drug and is therefore set aside as finished fluidextract.

By this time the bottles that had contained weak percolates Nos. 1 and 2 are empty, and as the next 250 cc. percolate drops, it is poured into bottle No. 1; the next batch into bottle No. 2, and so on until exhaustion, when we will have in the four original bottles weak percolates Nos. 1, 2, 3, and 4.

The percolation of batches Nos. 3 and 4, 250 Gm. each, of gentian, will be a repetition of the handling of batch No. 2. In both cases the first 250 cc. of percolate are set aside as finished fluidextract, and, when batch No. 4 is exhausted, the weak percolates Nos. 1, 2, 3, and 4, properly labeled, are placed in some dark, cool place, there to remain until the next time that the fluidextract must be made. The quantity given in above illustration is purely proportional and, of course, does not mean that 950 cc. fluidextract must be made each time. The 950 cc. of fluidextract—that is, the four portions 200 cc. plus 250 cc. plus 250 cc. plus 250 cc.—are to be carefully mixed and placed in proper container, and, of course, the next time the fluidextract is to be made from the weak percolates, the amount of the finished product will be 1000 cc.

This attractive and largely used process has been found by the writer and other investigators to have a fatal weakness. The assumption that the 950 cc. of so-called "fluidextract" contains the activity of 950 of the 1000 Gm. of drug used in the process cannot be verified on careful investigation. The amount of extractive in the 950 cc. depends on the skill of the operator and practically never in the writer's experiments did he obtain anything like the strength indicated.

In the present Pharmacopœia, repercolation is abandoned even as an alternative measure and in its place Type Process C—*fractional or divided percolation*—has been substituted. In this the 1000 Gm. of drug are divided into three portions of 500, 300, and 200 Gm. each. From the 500 Gm., 200 cc. of percolate are set aside as the reserved portion and 1500 cc. of weak percolate is then collected in portions of 300 cc. each. The 300 Gm. of drug is percolated with the weak percolates just suggested. The first 300 cc. of percolate are reserved; while 1000 cc. of weak percolate are collected in 200 cc. portions. These are used to percolate the last 200 Gm. of drug; 500 cc. of percolate being collected as reserve portion. Thus 1000 cc. of what is supposed to be finished fluidextract are obtained from 1000 Gm. of drug. Where an assay of the fluidextract is directed the final portion collected is 420 cc. The mixed percolates are then assayed and final adjustment of volume is made to bring the fluidextract to the proper strength.

Percolation with Incomplete Exhaustion.—In this process, 1000 Gm. of the drug are taken, moistened, packed and carefully percolated until 750 cc. of fluid are obtained. The marc is then thrown away and operation is discontinued.

This process assumes that the first 750 cc. of percolate from 1000 Gm. of drug will contain the activity of 750 Gm. of the drug employed. In the writer's investigation, such results were rarely obtained; he finding that 500 or at the most 600 cc. of percolate from a sample of drug contained in each cubic centimeter the activity of a gram of the drug. This process can be employed with good results, if the procedure given below is followed.

A sample of 50 Gm. of drug is percolated to exhaustion and the amount of extract is determined by evaporation of the percolate and weighing of the residue. Then 1000 Gm. of the same batch of drug is percolated until 500 cc. of percolate are obtained. Fifty cc. of this percolate is evaporated to dryness and the residue weighed and by comparison of the amount of extractive in the 500 cc. of percolate with the total extractive in the drug, as shown in the 50-Gm. sample, it is easy to calculate how much menstruum must be added to the 500 cc. of percolate in order to make it of true fluidextract strength.

Percolation and Maceration with Hydraulic Pressure.—This process was introduced by a firm of manufacturing pharmacists, but has been abandoned by them in favor of repercolation or fractional percolation, which is employed by almost all large manufacturers.

The process consists of taking a large quantity of the drug—say, 1000 kilos—macerating with a lesser quantity of menstruum—say, 300 liters—and, after a certain time, pressing this liquid by hydraulic pressure. The press cake is returned to the macerating vat, moistened with another 300 liters of liquid, which is pressed out. The process is then repeated with a sufficient quantity of menstruum, so that when it is pressed the third time the quantity of the expressed liquid, or official fluidextract, will amount to 1000 liters.

Preservation of Fluidextracts.—Fluidextracts keep well, as a rule, and the precipitate, often occurring, is usually inert. Do not think that home-made fluidextracts are poor because there is a sediment in them after a few months. The manufacturers' fluidextracts do the same thing, only they are kept in the factory long enough to allow complete precipitation; then they are filtered and bottled.

Billing and Perkins tried to solve the problem of precipitation by adjusting the fluidextract to an optimum (favorable) hydrogen-ion concentration. For Scoville's work on precipitation in tinctures, see p. 243.

It must be borne in mind, however, that in some cases the precipitate formed in fluidextracts contains a valuable constituent, and in this case the precipitate should be retained. Unfortunately, we have as yet no table showing us which precipitates should be retained and which rejected, and, therefore, at present it is customary always to dispense fluidextracts in a clear form. The Pharmacopœia directs that fluidextracts shall be preserved in tightly-closed containers and protected from direct sunlight or abnormal temperatures.

Acetic fluidextracts, or *acetracts,* are a line of fluidextracts prepared with 10 per cent acetic acid as a menstruum. This line never became very popular and with the dropping from the last Pharmacopœia of fluidextract of lobelia, acetic fluidextracts are no longer official.

SPECIAL NOTES ON THE OFFICIAL FLUIDEXTRACTS

The number of fluidextracts in the current Pharmacopœia has been reduced to eleven. There is so much sameness in most of them that what is said about one of them applies with equal force to almost all the others. Their strength is identical; their manufacture, as to minor details, is similar, with only a few exceptions. Their medical properties are those of the drugs from which they are derived, and will be left for discussion—as in all other galenics—until the constituent drug is considered. Their doses, which will be grouped at the close of this section, are usually the same as the constituent drug.

Hence they can be discussed in a comparatively small space, and instead of giving, as with the other galenics, a table of preparations followed by specific mention of each fluidextract, we can, after study of the general formula for fluidextracts given in the Pharmacopœia, present the data concerning most of the individual fluidextracts in tabular form. Before presenting the table, it should be noted that while in U.S.P. VIII there were 85 official fluidextracts, in U.S.P. X there were only 26 and in the U.S.P. XI this number has been further reduced to 11. Many of those deleted have been given recognition in the National Formulary which lists 71.

OFFICIAL FLUIDEXTRACTS MADE BY TYPE PROCESS, A. (See p. 259.)

FLUIDEXTRACTUM BELLADONNÆ RADICIS—Fluidextract of Belladonna Root

(Fldext. Bellad. Rad.)

Fluidextract of Belladonna Root yields, from each 100 cc., not less than 0.405 Gm. and not more than 0.495 Gm. of the alkaloids of belladonna root.

Alcohol Content.—66 to 71 per cent by volume.

Condensed Recipe. *

Belladonna root in No. 20 powder (1000 Gm.) is percolated with the menstruum, alcohol, 4 volumes; water, 1 volume. Of the percolate, the first 800 cc. are reserved, the rest is evaporated to a soft extract, which is dissolved in the reserved portion. After assay of a portion of this fluid, it is diluted with enough menstruum to make it the proper alkaloidal strength. For details, see U.S.P., p. 169.

Remarks.—This fluidextract is taken as the type simply because it is the first representative of the class appearing in the Pharmacopœia. In studying the recipe given above it will be found that the menstruum used throughout the process consists of alcohol, 4 volumes; water, 1 volume; that the drug is to be in a No. 20 powder and that 800 cc. of percolate are to be reserved. It will also be noted that in the case of alkaloidal drugs, the product, obtained when the soft extract is dissolved in the reserved portion, is assayed and is then diluted to the proper alkaloidal strength. In making fluidextracts of nonalkaloidal drugs, on the other hand, the liquid resulting from dissolving the soft extract in the reserved portion is immediately diluted with enough menstruum to make 1 liter. All these points are mentioned, since they form the basis of difference between this and the other fluidextracts of the same class. These other fluidextracts will be found below, grouped according to menstruum employed.

Dose.—0.05 cc. (3/4 minim).

FLUIDEXTRACTUM CANNABIS—Fluidextract of Cannabis

(Fldext. Cannab.)

Alcohol Content.—75 to 85 per cent by volume.

Condensed Recipe.

Cannabis in No. 40 powder (1000 Gm.) is percolated with alcohol after macerating forty-eight hours. Type Process A is followed to make 1000 cc. For details see U.S.P., p. 169.

Remarks.—Although a special bio-assay method was given for this fluidextract in the U.S.P. X, neither an assay process, nor a standard is given in the U.S.P. XI.

Dose.—0.1 cc. (1½ minims).

FLUIDEXTRACTUM ERIODICTYI—Fluidextract of Eriodictyon

(Fldext. Eriodict.—Fluidextract of Yerba Santa)

Alcohol Content.—57 to 62 per cent by volume.

Condensed Recipe.

Eriodictyon in No. 40 powder (1000 Gm.) is percolated with the menstruum, alcohol, 4 volumes, water, 1 volume, after macerating forty-eight hours. The first 800 cc. are reserved. Type process A is followed to make 1000 cc.

Dose.—1 cc. (15 minims).

OFFICIAL FLUIDEXTRACTS MADE BY TYPE PROCESS A

Menstruum.	Name.	Fineness of powder.	Remarks.
Alcohol, U.S.P.	Calendula (N.F. VI).	moderately fine.	
	Cannabis.	No. 40.	
Alcohol, 9 volumes; water, 1 volume	Apocynum (N.F. VI).	No. 40.	
	Buchu (N.F. VI)	No. 40.	
	Celery fruit (N.F. VI).	No. 40.	
	Cimicifuga (N.F. VI)	No. 40	
	Cotton root bark (N.F. VI).	No. 40.	
	Cubeb (N.F. VI).	No. 40,	
	Ginger.	No. 40	
	Jalap (N.F. VI).	No. 60	Percolated with sand; assay given.
Alcohol, 4 volumes; water, 1 volume	Belladonna root.	No. 20	Assay given.
	Buchu compound (N.F. VI).	No. 40.	
	Dioscorea (N.F. VI).	No. 40.	
	Echinacea (N.F. VI).	No. 40.	
	Eriodictyon.	No. 40.	
	Gelsemium (N.F. VI.).	No. 40.	
	Juniper (N.F. VI).	No. 20.	
	Rhubarb (N.F. VI).	No. 40.	
	Sabal (N.F. VI).	No. 40.	
	Serpentaria (N.F. VI).	No. 40.	
	Valerian (N.F. VI).	No. 40.	
Alcohol, 3 volumes; water, 1 volume	Arnica (N.F. VI).	No. 20	
	Belladonna leaf (N.F. VI).	No. 40.	Assay given.
	Caulophyllum (N.F. VI)	moderately fine.	
	Chionanthus (N.F. VI)	No. 40	
	Convallaria root (N.F. VI)	No. 40.	Assay given.
	Damiana (N.F. VI).	No. 40	
	Grindelia (N.F. VI).	No. 40	
	Guarana (N.F. VI).	No. 60.	
	Hyoscyamus (N.F. VI).	No. 20	Assay given.
	Leptandra (N.F. VI).	No. 40	
	Stillingia (N.F. VI)	No. 40	
	Stramonium (N.F. VI)	No. 40	Assay given.
	Trillium (N.F. VI).	No. 40.	
	Xanthoxylum (N.F. VI)	No. 40.	
Alcohol, 2 volumes; water, 1 volume	Calumba (N.F. VI)	No. 40	
	Colchicum corm (N.F. VI)	No. 40.	Assay given.
	Colchicum seed (N.F. VI).	No. 40	Drug first defatted with petroleum benzin; assay given.
	Humulus (N.F. VI)	No. 20	
	Hydrangea (N.F. VI).	No. 40	
	Hydrastis (N.F. VI).	No. 40	Assay given.
	Kola (N.F. VI).	moderately fine	Assay given.
	Senega (N.F. VI).	No. 40.	
	Viburnum opulus (N.F. VI).	No. 40.	
	Viburnum prunifolium (N.F. VI).	No. 40	
Diluted alcohol	Aletris (N.F. VI).	No. 40.	
	Berberis (N.F. VI).	No. 40.	
	Condurango (N.F. VI).	No. 40.	
	Euonymus (N.F. VI).	No. 40.	
	Euphorbia pilulifera (N.F. VI).	No. 40.	
	Gentian (N.F. VI).		
	Lappa (N.F. VI).	No. 40.	
	Oat (N.F. VI)	No. 40.	
	Phytolacca (N.F. VI).	No. 40.	
	Rhamnus cathartica (N.F. VI).	No. 40.	
	Sarsaparilla.	No. 20.	
	Trifolium (N.F. VI).	No. 40.	
	Uva ursi (N.F. VI).	No. 40.	
	Zea (N.F. VI).	finely cut.	
Alcohol, 1 volume; water, 2 volumes	Quassia (N.F. VI).	No. 40.	
	Senna.	No. 20.	
Alcohol, 1 volume; water, 3 volumes	Trifolium compound (N.F. VI).	No. 40.	

FLUIDEXTRACTUM SARSAPARILLÆ—Fluidextract of Sarsaparilla

(Fldext. Sarsap.)

Alcohol Content.—37 to 42 per cent by volume.

Condensed Recipe.

Sarsaparilla (1000 Gm.) in No. 20 powder is macerated forty-eight hours and percolated with a menstruum of diluted alcohol (U.S.P.). Type process A is followed to make 1000 cc.

Dose.—2 cc. (30 minims).

FLUIDEXTRACTUM SENNÆ—Fluidextract of Senna

(Fldext. Senn.)

Alcohol Content.—23 to 27 per cent by volume.

Condensed Recipe.

Senna (1000 Gm.) in No. 20 powder is macerated twenty-four hours and percolated with a menstruum of alcohol, 1 volume, water, 2 volumes. The first 800 cc. of percolate are reserved and type process A is followed to make 1000 cc.

Dose.—2 cc. (30 minims).

FLUIDEXTRACTUM ZINGIBERIS—Fluidextract of Ginger

(Fldext. Zingib.)

Fluidextract of Ginger contains, in each 100 cc., not less than 4.5 Gm. of ether-soluble extractive.

Alcohol Content.—69 to 76 per cent by volume.

Condensed Recipe.

Ginger (1000 Gm.) in No. 40 powder is macerated overnight and percolated with a menstruum of alcohol, 9 volumes, water, 1 volume. Type process A is followed to make 1000 cc.

Remarks.—This fluidextract is assayed for ether-soluble extractive by evaporating the fluidextract and extracting the residue with ether.

Dose.—0.6 cc. (10 minims).

OFFICIAL FLUIDEXTRACTS MADE BY TYPE PROCESS B

FLUIDEXTRACTUM NUCIS VOMICÆ N.F. VI—Fluidextract of Nux Vomica

(Fldext. Nuc. Vom.)

Fluidextract of Nux Vomica contains, in each 100 cc., not less than 1.05 Gm. and not more than 1.25 Gm. of strychnine.

Alcohol Content.—57 to 63 per cent by volume.

Condensed Recipe.

Nux vomica in a No. 40 powder (1000 Gm.) is percolated with the initial menstruum—acetic acid, 2 volumes; water, 3 volumes; alcohol, 15 volumes—and then with the final menstruum—alcohol, 3 volumes; water, 1 volume. Reserve the first 850 cc. of percolate, recover the alcohol from the remainder, evaporate it to a soft extract which is then dissolved in the reserved portion. The resulting fluid is then assayed and is then diluted to the proper strength with the final menstruum. For details, see N.F., p. 173.

Remarks.—None of the U.S.P. fluidextracts are made by Type Process B. Hence we depart from our usual custom of describing a U.S.P. preparation as the typical example in this place. The fluidextracts made with menstrua containing glycerin or acid are placed in a class separate from those made with purely hydro-alcoholic menstrua, because there is a slight difference in the method of manipulation. As seen in the above typical recipe, in making 1000 cc. of the fluidextract, only the first menstruum contains the acid; the rest of the menstruum required being merely alcohol and water. This necessitates, in the table given below, two columns for menstrua, the column headed "final menstruum" being that employed after the first 1000 cc. of menstruum (if 1000 Gm. of drug are being percolated) are used up. Bear in mind that if repercolation is used, the first (glycerinic or acid) menstruum is used through the entire operation.

Dose.—0.1 cc. (1½ minim).

OFFICIAL FLUIDEXTRACTS MADE BY TYPE PROCESS B

Menstruum.	Name.	Fineness of powder.	Final menstruum.	Remarks.
Alcohol, 15; water, 3; acetic acid, 2	Nux vomica (N F. VI).	No. 40.	Alcohol, 3; water, 1.	Assay given.
Alcohol, 15; water, 4; hydrochloric acid, 1	Sanguinaria (N.F. VI).	No. 40.	Alcohol, 3; water, 1.	
Alcohol, 10; water, 9; acetic acid, 1	Lobelia (N F VI).	No 40.	Diluted alcohol.	
Alcohol, 9; glycerin, 1	Castanea (N F VI).	No. 40.	Alcohol.	
	Hamamelis leaf (N.F. VI).	No. 40.	Alcohol.	
	Krameria (N.F. VI).	moderately fine.	Alcohol.	
Alcohol, 5; water, 4; glycerin, 1	Rose (N.F. VI).	No. 40.	Diluted alcohol.	
	Sarsaparilla compound (N.F. VI).	No. 40.	Diluted alcohol.	
	Taraxacum (N.F. VI).	No. 40.	Diluted alcohol.	
Glycerin, 1; water 2, followed by alcohol, 2; water, 1.	Wild cherry (N.F. VI).	No. 20.	Alcohol, 1; water, 3	
Alcohol, 1; water, 2; glycerin, 1	Thyme (N.F. VI).	No. 40.	Alcohol, 1; water, 3.	

In making fluidextracts of alkaloidal drugs of this class, the liquid obtained by dissolving the soft extract in the reserved portion of the percolate is assayed and is then diluted with the menstruum to the proper alkaloidal strength.

It will be noticed that fluidextract of nux vomica, sanguinaria, and lobelia (see above) are prepared with an initial menstruum containing acid; this being added to fix and to hold in solution, the alkaloid characteristic to the drug.

OFFICIAL FLUIDEXTRACTS MADE BY TYPE PROCESS C

FLUIDEXTRACTUM ERGOTÆ—Fluidextract of Ergot

(Fldext. Ergot.—Extractum secalis cornuti fluidum acidum P.I.)

Fluidextract of Ergot, when assayed by the method given in U.S.P. XI., pp. 171 and 148, possesses a potency, per cubic centimeter, equivalent to not less than 0.5 mg. of ergotoxine ethanesulfonate.

Alcohol Content.—37 to 42 per cent by volume.

Condensed Recipe.

Ergot (1000 Gm.) in No. 20 powder, recently ground is extracted with purified petroleum benzin until a few drops of percolate leave no greasy stain on filter paper. The drug is then dried by exposure to air. A fluidextract is prepared by type process C, using a menstruum of hydrochloric acid, 2 volumes; diluted alcohol (U.S.P.), 98 volumes and obtaining 1000 cc. of product. An alternative process for removing the fat is permitted. This involves chilling the finished fluidextract to −14° C. and filtering out the congealed fat. An assay process is prescribed. For details see U.S.P., p. 171.

Dose.—2 cc. (30 minims).

OFFICIAL FLUIDEXTRACTS MADE BY TYPE PROCESS C

Name.	Menstruum	Fineness of powder.	Remarks
Aconite (N.F. VI). . .	Alcohol, 3 volumes; water, 1 volume.	No. 40.	
Ergot.	Diluted alcohol, 98 volumes; hydrochloric acid, 2 volumes.	No. 20	Drug defatted with petroleum benzin, assay given.

OFFICIAL FLUIDEXTRACTS MADE BY TYPE PROCESS D

FLUIDEXTRACTUM CASCARÆ SAGRADÆ—Fluidextract of Cascara Sagrada

(Fldext. Cascar. Sagr.—Fluid Extract of Rhamnus Purshiana)

Alcohol Content.—20 to 24 per cent by volume.

Condensed Recipe.

Cascara sagrada, in No. 20 powder (1000 Gm.), is mixed with 3000 cc. of boiling water; is macerated for two hours and is percolated, enough boiling water being used to exhaust the drug. The percolate is evaporated to 750 cc. and then 250 cc. of alcohol are added. For details see U.S.P., p. 170.

Remarks.—This preparation is representative of those fluidextracts which are prepared by percolating the drug with boiling water, followed by the evaporation of the percolate to the proper volume, after which enough alcohol is added to preserve the finished product.

Aromatic fluidextract of cascara sagrada and **fluidextract of glycyrrhiza** belong in the class of aqueous fluidextracts preserved with alcohol, but the methods by which they are prepared are sufficiently different to justify giving each special attention below.

OFFICIAL FLUIDEXTRACTS MADE BY TYPE PROCESS D

Menstruum.	Name.	Fineness of powder.	Remarks.
Boiling water.	Cascara sagrada.	No. 20.	
Boiling water	Frangula (N.F. VI).	No 20.	
Boiling water . . .	Glycyrrhiza.	No. 20	Percolate boiled with ammonia water.
Boiling water	Triticum (N.F VI).	Finely cut.	

SPECIAL FLUIDEXTRACTS

Under this heading are grouped the few remaining official fluidextracts which either do not lend themselves to the grouping followed on the preceding pages, or possess some peculiarity worthy of special mention.

FLUIDEXTRACTUM CASCARÆ SAGRADÆ AROMATICUM—Aromatic Fluidextract of Cascara Sagrada

(Fldext. Casc. Sagr. Arom.—Aromatic Fluid Extract of Rhamnus Purshiana)

Alcohol Content.—17 to 19 per cent by volume.

Condensed Recipe.

Ingredients.—Cascara sagrada, 1000 Gm. in No. 20 powder; magnesium oxide, 120 Gm.; pure extract of glycyrrhiza, 40 Gm.; alcohol, 200 cc.; saccharin, 2 Gm.; oil of anise, 0.65 cc.; oil of coriander, 0.15 cc.; methyl salicylate, 0.1 cc.; boiling water, enough to make 1 liter.

Manipulation.—Mix the cascara sagrada with the magnesium oxide and with 2000 cc. of boiling water. Macerate forty-eight hours, percolate with boiling water to exhaustion. Evaporate percolate to 750 cc., and add the other ingredients. For details see U.S.P., p. 170.

Remarks.—This fluidextract is made by Type Process D, all general details being like the other fluidextracts of this class. The important distinction is the treatment of the drug, before percolating, with magnesium oxide, this being done to remove most of the bitter taste from the cascara sagrada (p. 894). This device lessens the activity of the product since some of the purgative principle is removed by reaction with the magnesia. Note, of course, the constituents added to make the product true to its name, "aromatic," these constituents being extract of glycyrrhiza; oils of anise, and coriander; and methyl salicylate.

FLUIDEXTRACTUM GLYCYRRHIZÆ—Fluidextract of Glycyrrhiza

(**Fldext. Glycyrrh.**—Fluidextract of Licorice Root)

Alcohol Content.—20 to 24 per cent by volume.

Condensed Recipe.

Moisten glycyrrhiza (1000 Gm.) in No. 20 powder with 3000 cc. of boiling water. Then percolate with boiling water to exhaustion. Add ammonia water and boil until the volume is reduced to 1500 cc., filter and evaporate the filtrate to 750 cc. and when cool add 250 cc. of alcohol and enough water to make 1 liter. For details see U.S.P., p. 172.

Remarks.—This fluidextract is now made by Process D. In the U.S.P. IX formula the drug was first extracted with water containing ammonia water, the first portion of the percolate was reserved, the balance was evaporated to a soft extract, which was dissolved in the reserved portion. In the U.S.P. X formula no ammonia water was used. The amount of alcohol added to the product (250 cc.) was to insure the stability of the finished fluidextract. This type of fluidextract of glycyrrhiza, whether prepared by the method of U.S.P. IX or of U.S.P. X, is similar to the popular commercial forms intended "for quinine mixtures," and is much superior to the alcoholic fluidextract of the Pharmacopœia of 1890.

FLUIDEXTRACTUM IPECACUANHÆ—Fluidextract of Ipecac

(**Fldext. Ipecac.**)

Fluidextract of Ipecac yields, from each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of the ether-soluble alkaloids of ipecac.

Alcohol Content.—28 to 33 per cent by volume.

Condensed Recipe.

Ipecac (1000 Gm.) in No. 60 powder is macerated seventy-two hours and percolated with a menstruum of alcohol, 3 volumes; water, 1 volume until the drug is exhausted. The entire percolate is then reduced to 1000 cc. by evaporation at 60° C. To this 2000 cc. of water are added and after standing overnight the mixture is filtered and filtrate evaporated to 565 cc., after which 35 cc. of hydrochloric acid and 300 cc. of alcohol are added. After assaying a portion of the fluidextract, adjustment is made with a mixture of alcohol, 30 volumes; hydrochloric acid, 3.5 volumes, and water, 66.5 volumes to bring the finished product to the required strength. For details see U.S.P., pp. 172 and 173.

Dose.—Expectorant, 0.06 cc. (1 minim); emetic, 1 cc. (15 minims).

Compound Fluidextract of Buchu (N.F. VI) is made from ground buchu, cubeb, juniper and uva ursi, by Type Process A; the menstruum being 4 volumes of alcohol and 1 volume of water. *Dose.*—2 cc. (30 minims).

Aqueous Fluidextract of Cinchona (N.F. IV) is prepared by percolating red cinchona with water containing glycerin and hydrochloric acid. The manipulation resembles Type Process B; the final menstruum being water. To the concentrated percolate, there is added enough alcohol to preserve it. It should contain 4.5 to 5.5 per cent of cinchona alkaloids. It resembles Battley's Liquid Cinchona, a preparation that was very popular in England and this country thirty years ago. *Dose.*—1 cc. (15 minims).

Compound Fluidextract of Sarsaparilla (U.S.P. IX; N.F. VI) is made by Type Process B, percolating sarsaparilla (750 Gm.); glycyrrhiza (120 Gm.); sassafras (100 Gm.); and mezereum (30 Gm.) first with the menstruum—glycerin, 100 cc.; alcohol, 500 cc.; water, 400 cc.; then with diluted alcohol. Note carefully the ingredients, especially that it does not contain the same constituents as the compound syrup of sarsaparilla, and it must in no instance, therefore, be used in preparing the official compound syrup.

Fluidextractum Scillæ (U.S.P. X; N.F. VI) or *Fluidextract of Squill* is a biologically assayed preparation. It is made as follows: Squill, in No. 40 powder (1000 Gm.) is moistened with the menstruum—alcohol, 2 volumes; water, 1 volume. The moist drug is macerated forty-eight hours and is percolated with the menstruum. Concentrate the percolate by evaporation under reduced pressure at a temperature not exceeding 45° C. to about three fourths the finished volume. This is mixed with four times its volume of alcohol, and allowed to stand two or three days. The clear liquid is decanted; the residue washed and resulting combined liquids distilled (to recover the alcohol) and is concentrated to a soft extract which is dissolved in a sufficient amount of alcohol (525 volumes) and water (475 volumes) to make a fluidextract after adjustment to the biological standard. This fluid is then assayed and diluted to the proper strength by addition of diluted alcohol. For details see N.F., p. 177. It will be noticed that in the recipe just given, the squill is percolated with a hydro-alcoholic menstruum; that the entire percolate is then concentrated (the alcohol being recovered); and that the concentrated aqueous fluid is mixed with alcohol, in order to precipitate the mucilaginous matter that was contained in the percolate. The filtrate and strongly alcoholic washings are again concentrated, and enough diluted alcohol is added to the concentrate to make the finished fluidextract a stable product. *Dose.*—0.1 cc. (1½ minims).

Fluidextractum Senegæ (U.S.P. X; N.F. VI) or *Fluidextract of Senega* is made from senega, in No. 40 powder by Type Process A. Enough ammonia is added to make the product faintly alkaline. This fluidextract is prepared with a menstruum containing ammonia, the drug being percolated with a hydro-alcoholic menstruum and ammonia water being added after percolation. Senega contains pectinous material (p. 722) and ammonia is employed to prevent gelatinization of the finished fluidextract. It will be noticed that the official recipe resembles Type Process A and that like fluidextract of glycyrrhiza the alcohol employed is chiefly for preservative.

Compound Fluidextract of Stillingia (N.F. V) is prepared from stillingia, corydalis, iris, sambucus, chimaphila, coriander and xanthoxylum berries, by Type Process A. The menstruum is diluted alcohol. *Dose.*—2 cc. (30 minims).

Compound Fluidextract of Trifolium (N.F. VI) is made by Type Process A from trifolium, glycyrrhiza, berberis, cascara amarga, lappa, phytolacca, stillingia and xanthoxylum, using as menstruum, alcohol, 1; water, 3. *Dose.*—4 cc. (1 fluidrachm).

Fluidextract of Wild Cherry (N.F. VI) is made by moistening wild cherry bark with a mixture of glycerin, 1 volume and water, 2 volumes; then with a mixture of alcohol, 2 volumes and water, 1 volume. The moistened drug is then percolated with 1 volume of alcohol and 3 volumes of water and the fluidextract is finished by what is practically Type Process B. *Dose.*—2 cc. (30 minims).

FLUIDEXTRACTS OF THE NATIONAL FORMULARY

NOTE.—The Type Processes, A, B, C, and D are the same as those of the Pharmacopœia. Instead of Latin and English names, the name of the drug only is given.

Name.	Type process.	First menstruum.	Final menstruum.	Remarks (figures indicate dose).
Aconite	C	Alcohol 3; water, 1.	None.	Assay given, 0.06 cc. (1 minim).
Aletris	A	Diluted alcohol.	None.	2 cc. (30 minims).
Apocynum	A	Alcohol, 9; water, 1.	None.	0.2 cc. (3 minims). Use cautiously.
Arnica	A	Alcohol, 3; water, 1.	None.	0.1 cc. (1½ minims).
Avena	A	Diluted alcohol.	None.	4 cc. (1 fluidrachm).
Belladonna leaf	A	Alcohol, 3; water, 1.	None.	Assay given. 0.06 cc. (1 minim).
Berberis	A	Diluted alcohol.	None.	2 cc. (30 minims).
Buchu	A	Alcohol, 9; water, 1.	None.	2 cc. (30 minims).
Buchu compound	A	Alcohol, 4; water, 1.	None.	2 cc. (30 minims).
Calendula	A	Alcohol.	None.	1 cc. (15 minims).
Calumba	A	Alcohol, 2; water, 1.	None.	1 cc. (15 minims).

FLUIDEXTRACTS OF THE NATIONAL FORMULARY—(*Continued*)

Name.	Type process.	First menstruum.	Final menstruum.	Remarks (figures indicate dose).
Caulophyllum	A	Alcohol, 3; water, 1.	None.	0.5 cc. (8 minims).
Celery fruit	A	Alcohol, 9; water, 1.	None.	2 cc. (30 minims).
Chestnut leaves	B	Alcohol, 9; glycerin, 1.	Alcohol.	4 cc. (1 fluidrachm).
Chionanthus	A	Alcohol, 3; water, 1.	None.	2 cc. (30 minims).
Cimicifuga	A	Alcohol, 9; water, 1.	None.	1 cc. (15 minims).
Colchicum corm	A	Alcohol, 2; water, 1.	None.	Assay given. 0.25 cc. (4 minims).
Colchicum seed	A	Alcohol, 2; water, 1.	None.	Assay given. 0.2 cc. (3 minims).
Condurango	A	Diluted alcohol.	None.	4 cc. (1 fluidrachm).
Convallaria root	A	Alcohol, 3; water, 1.	None.	Assay given. 0.2 cc. (3 minims).
Cotton root bark	A	Alcohol, 9; water, 1.	None.	2 cc. (30 minims).
Cubeb	A	Alcohol, 9; water, 1.	None.	2 cc. (30 minims).
Damiana	A	Alcohol, 3; water, 1.	None.	2 cc. (30 minims).
Dioscorea	A	Alcohol, 4; water, 1.	None.	4 cc. (1 fluidrachm).
Echinacea	A	Alcohol, 4; water, 1.	None.	1 cc. (15 minims).
Euonymus	A	Diluted alcohol.	None.	0.5 cc. (8 minims).
Euphorbia pilulifera	A	Diluted alcohol.	None.	2 cc. (30 minims).
Frangula	D	Water; alcohol as preservative.	None.	1 cc. (15 minims).
Gelsemium	A	Alcohol, 4; water, 1.	None.	0.03 cc. (½ minim).
Gentian	A	Diluted alcohol.	None.	1 cc. (15 minims).
Grindelia	A	Alcohol, 3; water, 1.	None.	2 cc. (30 minims),
Guarana	A	Alcohol, 3; water, 1.	None.	Assay given. 2 cc. (30 minims).
Hamamelis leaf	B	Glycerin, 100; alcohol, 900.	Alcohol.	2 cc. (30 minims).
Hops	A	Alcohol, 2; water, 1.	None.	2 cc. (30 minims).
Hydrangea	A	Alcohol, 2; water, 1.	None.	2 cc. (30 minims).
Hydrastis	A	Alcohol, 2, water, 1.	None.	Assay given 2 cc. (30 minims).
Hyoscyamus	A	Alcohol, 3; water, 1.	None.	Assay given. 0.2 cc. (3 minims).
Jalap	A	Alcohol, 9; water, 1.	None.	Sand used in percolation, 1 cc. (15 minims). Assay given.
Juniper	A	Alcohol, 4; water, 1.	None.	4 cc. (1 fluidrachm).
Kola	A	Alcohol, 2; water, 1.	None.	Assay given. 4 cc. (1 fluidrachm).
Krameria	B	Glycerin, 100; alcohol, 900.	Alcohol.	1 cc. (15 minims).
Lappa	A	Diluted alcohol	None.	2 cc. (30 minims).
Leptandra	A	Alcohol, 3; water, 1.	None.	1 cc. (15 minims).
Lobelia	B	Acetic acid, 50, alcohol, 500; water, 450.	Diluted alcohol.	0.1 cc. (1½ minims).
Nux Vomica	B	Alcohol, 15; water, 3; acetic acid, 2.	Alcohol, 3 water, 1.	Assay given. 0.1 cc. (1½ minims).
Phytolacca	A	Diluted alcohol.	None.	Dose, as alterative, 0.1 cc. (1½ minims).
Quassia	A	Alcohol, 1; water, 2.	None.	0.5 cc. (8 minims).
Rhamnus cathartica	A	Diluted alcohol.	None.	1 cc. (15 minims).
Rhubarb	A	Alcohol, 4, water, 1.	None.	1 cc. (15 minims).
Rose	B	Glycerin, 1; alcohol, 5; water, 4.	Diluted alcohol.	2 cc. (30 minims).
Sabal	A	Alcohol, 4; water, 1.	None.	1 cc. (15 minims).
Sanguinaria	B	Hydrochloric acid, 50; water, 200; alcohol, 750.	Alcohol, 3; water, 1.	0.25 cc. (2 minims).
Sarsaparilla, compound	B	....	....	See p 270.
Senega	A	Alcohol, 2; water, 1.	None.	1 cc (15 minims).
Serpentaria	A	Alcohol, 4; water, 1.	None.	1 cc (15 minims).
Squill	Special.	Alcohol, 2; water, 1.		Assay given. 0.1 cc. (1½ minims).
Stillingia	A	Alcohol, 3; water, 1.	None.	2 cc. (30 minims).
Stramonium	A	Alcohol, 3; water, 1.	None.	0.075 cc. (1¼ minims).
Taraxacum	B	Glycerin, 100; alcohol, 500; water, 400.	Diluted alcohol.	4 cc. (1 fluidrachm).
Thyme	B	Glycerin, 100; alcohol, 100; water, 200.	Alcohol, 1; water, 3.	4 cc. (1 fluidrachm).
Trifolium	A	Diluted alcohol.	None.	4 cc. (1 fluidrachm).
Trifolium compound	A	....	....	See p. 270.
Trillium	A	Alcohol, 3; water, 1.	None.	2 cc. (30 minims)
Triticum	D	Water; alcohol as a preservative.	None.	10 cc. (2½ fluidrachms).
Uva Ursi	A	Diluted alcohol.	None.	2 cc. (30 minims).
Valerian	A	Alcohol, 4; water, 1.	None.	1 cc. (15 minims).
Viburnum opulus	A	Alcohol, 2; water, 1.	None.	2 cc. (30 minims).
Viburnum prunifolium	A	Alcohol, 2; water, 1.	None.	2 cc. (30 minims).
Wild cherry	B	Glycerin, 1, water, 2, followed by alcohol, 2; water, 1.	Alcohol, 1; water, 3.	2 cc. (30 minims).
Xanthoxylum	A	Alcohol, 3; water, 1.	None.	2 cc. (30 minims).
Zea	A	Diluted alcohol.	None.	4 cc. (1 fluidrachm).

LABORATORY EXERCISES

DRUG GRINDING

Reduce gentian root by means of mill or iron mortar to a No. 30 powder, using a No. 30 sieve in the work. Take 50 Gm. of the powder and make into a neat package. (See p. 313.)

MAKE FLUIDEXTRACT OF GENTIAN

Gentian	50 Gm.
Diluted alcohol, U.S.P.	q.s.

Put drug into pint evaporating dish, and moisten with 50 cc. dilute alcohol; put into 8-ounce wide-mouthed bottle, cork, and let stand forty-eight hours. Then percolate.

PERCOLATION

Take percolator, put cork and percolating tubing (p. 186) into neck, and pour water in to see if it leaks. If it does not leak, pour out water, remove the cork and tubing and wipe percolator dry; insert plug of cotton in neck of percolator and a layer of cotton on that. Then pour in the moist gentian and pack firmly with gentle and uniform pressure. Then cut a piece of filter paper so as to fit inside the percolator, and place this on top of the packed drug, laying a piece of glass—glass stopper—on top to hold the paper down. Then fit the rubber tubing and cork to percolator again, place percolator on ring (p. 186) pour on the drug 100 to 150 cc. diluted alcohol, and cover top of percolator in some way to prevent evaporation. Place percolator tubing into 8-ounce wide-mouthed bottle, which has been previously graduated to 40 cc. Let percolation proceed at the rate of 2 to 5 drops a minute, regulating the flow by raising the receiver if it runs too rapidly, or lowering same if it runs too slowly. When 40 cc. of percolate have dropped through, let the percolate drop into pint flask and cork the wide-mouthed bottle containing first percolate, labeling it "reserved portion." Continue percolating into pint flask until the drug is exhausted (perhaps more than a pint of percolate will be necessary), and when this is accomplished, cork the pint flask and label "weak percolate." It is needless to say that as the first menstruum (the dilute alcohol) passes through the drug, more menstruum is poured on, care being taken always to have some menstruum covering the drug. When the drug is exhausted, the weak percolate is to be distilled.

Remarks.—*Percolation.*—For full description, see p. 186.

Testing Percolator Fittings.—This is essential, for if the tube leaks the percolation will prove a messy business.

Plug with Cotton.—This can best be done with a long glass rod or tube, though a piece of wire answers. The percolator must be perfectly dry.

Handling the Drug.—*Grind to only No. 30 powder,* because the cells of gentian are large, and most of them are ruptured when in No. 30 powder. (See p. 137.)

Moistened before packing, so as to permit the drug cells to swell. If put in percolator dry and menstruum then poured on, the drug swells so much that percolation is impeded. (See p. 187.)

Pack Drug Evenly.—If one side is packed more loosely than the other, the menstruum will run down the looser side, and that tightly packed will not be exhausted. Uneven packing is shown in the descent of the first menstruum through the drug. Should pass down in a perfect ring. (See p. 187.)

Percolation.—*Do not pack too tightly,* else the percolate will drop too slowly. Sometimes, under these circumstances, the percolate refuses to drop, and the only thing to do is to empty out drug and pack again. Sometimes the percolate can be "coaxed" into dropping by applying suction at end of tube, or by filling percolator with menstruum. If the first 40 cc. of heavy percolate can be gotten through, the lighter weak percolate will usually run without trouble.

Filter paper on top, to keep upper layer of powder from floating to top of menstruum. Glass weight holds the filter paper down.

Reserve First 40 cc.—If properly percolated the first 40 cc. is supposed to contain the soluble principles of about 40 Gm. of drug.

Percolate to Exhaustion.—The remaining strength of the 40 Gm. of drug is hard to remove, requiring about ten times the amount of menstruum as does the reserved portion. Percolate until the drops of liquid are only a faint straw color and almost devoid of bitterness.

Menstruum.—The solvent used in exhausting drug. In this case the menstruum is diluted alcohol, U.S.P.—equal volumes of alcohol and water.

Keep Drug Covered with Menstruum.—If not, the menstruum in the upper layers evaporates, leaving fissures, and when fresh menstruum is poured on, it will run through the fissures rather than through the drug.

Distillation of Weak Percolate.—Fit pint flask about half filled with weak percolate with a cork, bore hole through cork with rat-tail file or with cork-cutter, and in this hole snugly fit a piece of glass tubing bent to an angle of 60 degrees; pass the other end of this tube through hole in a cork, fitting into neck of Liebig condenser.

Immerse flask in water bath, preventing direct contact with bottom by having it rest on wad of paper. Connect flask and condenser, fastening latter in place with appropriate clamps, and pass a stream of water through condenser, entering from the lower end and emerging from top.

Start heat under water bath and continue lively heat, replenishing water in bath when necessary. Collect distillate in second pint flask, and continue distillation until over half of the weak percolate has distilled over. Then pour residue in pint evaporating dish, and evaporate on water bath with constant stirring until residue is of the consistency of soft extract.

Remarks.—Rig up distilling apparatus as on p. 113.

For glass bending and cork boring, see p. 115.

Condensing water run in lower end of condenser—not the upper end, as the heated water rises and must be removed from highest level.

Only about three fourths of the percolate is distilled, since percolate is only half alcohol, and that is what we wish to save. Since the water is of no value, we evaporate it in open air, as it will evaporate more quickly that way than by distillation.

The *alcoholic strength of the distillate* can be estimated by taking its specific gravity and referring to alcohol table in the Pharmacopœia.

Do not have the distilling flask full of percolate, as it will distil too slowly or froth over into condenser. If you have a pint of percolate or over, add same to distilling flask in portions, pouring in new portions as that part already in flask has evaporated.

Evaporate Residue with Constant Stirring.—Remember that the residue is now aqueous, and that you cannot *boil* water on a water bath. Remember that evaporation below the boiling point can be rapidly accomplished only by constant stirring. If the dish is left on water bath without stirring, the evaporation will be very slow.

Finishing.—The soft extract is dissolved in the reserve portion, and the mixture poured into a graduate. The evaporating dish is washed out with about 5 cc. diluted alcohol, and this poured into the graduate, and then enough diluted alcohol is added to make finished fluidextract measure 50 cc. The mixture is thoroughly stirred, and so made constitutes Fluidextract of Gentian, N.F.

Remarks.—*The weak percolate is evaporated to soft extract*—most of the water is driven from it—lest that water precipitate some of the principles dissolved in the reserved portion.

The *finished fluidextract* is usually filtered after standing some months. All large manufacturers let their fluidextracts thus "age" for from six months to a year, so that when bottled and shipped, no further precipitation is apt to occur.

DOSES OF OFFICIAL FLUIDEXTRACTS

0.05 cc. (¾ minim).......	Fluidextract of belladonna root.
0.03 cc. (½ minim).........	Fluidextract of gelsemium (N.F. VI).
0.06 cc. (1 minim)..........	Fluidextracts of aconite (N.F. VI), belladonna leaf (N.F. VI), and ipecac (N.F. VI) (as an expectorant).
0.075 cc. (1¼ minims)......	Fluidextract of stramonium (N.F. VI).
0.1 cc. (1½ minims)........	Fluidextracts of arnica (N.F. VI), cannabis, lobelia (N.F. VI), nux vomica (N.F. VI), phytolacca (N.F. VI) (as an alterative) and squill (N.F. VI).
0.125 cc. (2 minims)........	Fluidextract of sanguinaria (N.F. VI).
0.2 cc. (3 minims)..........	Fluidextracts of apocynum (N.F. VI), colchicum seed (N.F. VI), convallaria root (N.F. VI), and hyoscyamus (N. F. VI).
0.25 cc. (4 minims).........	Fluidextract of colchicum corm (N.F. VI).
0.5 cc. (8 minims)..........	Fluidextracts of caulophyllum (N.F. VI), euonymus (N. F. VI), and quassia (N.F. VI).
0.6 cc. (10 minims).........	Fluidextract of ginger.
1 cc. (15 minims)..........	Fluidextracts of cascara sagrada, calendula (N.F. VI), calumba (N.F. VI), cimicifuga (N.F. VI), echinacea (N.F. VI), eriodictyon, frangula (N.F. VI), gentian (N.F. VI), ipecac (N.F. VI) (as an emetic), jalap (N.F. VI), krameria (N.F. VI), leptandra (N.F. VI), phytolacca (N.F. VI) (as an emetic), rhamnus cathartica (N.F. VI), rhubarb (N.F. VI), sabal (N.F. VI), senega (N.F. VI), serpentaria (N.F. VI) and valerian (N.F. VI).

2 cc. (30 minims)..........	Fluidextracts of aletris (N.F. VI), cascara sagrada aromatic, celery fruit (N.F. VI), cotton root bark (N.F. VI), berberis (N.F. VI), buchu (N.F. VI), buchu compound (N.F. VI), chionanthus (N.F. VI), cubeb (N.F. VI), damiana (N.F. VI), ergot, euphorbia pilulifera (N.F. VI), glycyrrhiza, grindelia (N.F. VI), guarana (N.F. VI), hamamelis leaf (N.F. VI), humulus (N.F. VI), hydrangea (N.F. VI), hydrastis (N.F. VI), lappa (N.F. VI), rose (N.F. VI), sarsaparilla, sarsaparilla compound (N.F. VI), senna, stillingia (N.F. VI), trillium (N.F. VI), uva ursi (N.F. VI), viburnum opulus (N.F. VI), viburnum prunifolium (N.F. VI), wild cherry (N.F. VI), and xanthoxylum (N.F. VI).
4 cc. (1 fluidrachm)........	Fluidextracts of castanea (N.F. VI), condurango (N.F. VI), dioscorea (N.F. VI), juniper (N.F. VI), kola (N.F. VI), oat (N.F. VI), taraxacum (N.F. VI), thyme (N.F. VI), trifolium (N.F. VI), trifolium compound (N.F. VI), and zea (N.F. VI).
10 cc. (2½ fluidrachms).....	Fluidextract of triticum (N.F. VI).

OFFICIAL FLUIDEXTRACTS DIRECTED TO BE ASSAYED, CHEMICALLY

Fluidextract	*Assayed strength*
Belladonna leaf (N.F. VI)...	0.27 to 0.33 per cent alkaloids of belladonna leaf.
Belladonna root..........	0.405 to 0.495 per cent alkaloids of belladonna root.
Colchicum corm (N.F. VI)..	0.31 to 0.39 per cent of colchicine.
Colchicum seed (N.F. VI)...	0.4 to 0.5 per cent of colchicine.
Guarana (N.F. VI).........	3.6 to 4.4 per cent of anhydrous caffeine.
Hydrastis (N.F. VI)........	2.25 to 2.75 per cent ether-soluble alkaloids of hydrastis.
Hyoscyamus (N.F. VI).....	0.035 to 0.045 per cent alkaloids of hyoscyamus.
Ipecac	1.8 to 2.2 per cent ether-soluble alkaloids of ipecac.
Jalap (N.F. VI)............	8.5 to 9.5 per cent resin of jalap.
Kola (N.F. VI)............	0.85 to 1.15 per cent anhydrous caffeine.
Nux vomica (N.F. VI)......	1.05 to 1.25 per cent of strychnine.
Stramonium (N.F. VI).....	0.25 to 0.35 per cent alkaloids of stramonium.

OFFICIAL FLUIDEXTRACTS DIRECTED TO BE ASSAYED, BIOLOGICALLY

Fluidextract	*Standard*
Aconite (N.F. VI)..........	Mortality of guinea-pigs checked against a solution of 15 mg. of reference aconitine in 100 cc. of 70 per cent alcohol.
Convallaria root (N.F. VI)..	0.1 Gm. is equivalent to not less than 2.75 and not more than 3.25 U.S.P. Digitalis Units.
Ergot....	Assay based upon the darkening of a cock's comb checked against a freshly prepared 1 : 100 aqueous solution of tartaric acid containing 0.5 mg. of ergotoxine ethanesulfonate per cubic centimeter.
Squill (N.F. VI)...........	Potency per cubic centimeter equivalent to not less than 0.80 mg. and not more than 0.90 mg. of standard ouabain.

FLUIDGLYCERATES

This is a class of glycerinic fluidextracts suggested by Beringer, in which instead of alcohol and water, a mixture of glycerin, 500 cc. and water, 1500 cc. is employed as the first menstruum and chloroform water as the final menstruum; the manipulation being similar to Type Process B used in making fluidextracts. They contain approximately 50 per cent by volume of glycerin and represent in each cubic centimeter the activity of 1 Gm. of the drug employed. Only a general formula is given in the National Formulary for fluidglycerates. Special recipes were provided for the following in the N.F. V.

Fluidglycerate of Cascara Sagrada, prepared as outlined above from cascara sagrada in No. 20 powder.

Aromatic Fluidglycerate of Cascara Sagrada, prepared by treating cascara sagrada with lime and magnesium oxide (see p. 893) after which it is percolated with the glycerinic menstruum and then with chloroform water; and a concentrated liquid preparation of bitterless cascara sagrada is obtained by manipulation resembling Type

Process B. This concentrate is then mixed with fluidglycerate of glycyrrhiza and with oils of fennel, clove and cinnamon; the finished preparation being adjusted so that each liter represents the strength of 750 Gm. of cascara sagrada and 250 Gm. of glycyrrhiza.

Fluidglycerate of Glycyrrhiza is prepared by exhausting the drug (1000 Gm.) with boiling water, the aqueous percolate being evaporated to 500 cc. mixed with 500 cc. glycerin and enough water to make 1 liter.

Fluidglycerate of Krameria is prepared from krameria in No. 20 powder, as per general formula given above.

Fluidglycerate of Rhubarb is similarly prepared.

WINES

Wines are alcoholic fluids prepared from drugs by the processes of solution, maceration or percolation, differing from tinctures only in the solvent employed; wine being used instead of various strengths of alcohol. While wines represent one of the oldest forms of liquid pharmaceutical preparations, the eight recognized in U.S.P. VIII were dropped during the ninth revision along with the basic fluids, red wine and white wine; since it was claimed that tinctures and fluidextracts covered the therapeutic needs as far as alcoholic pharmaceuticals are concerned. N.F. IV recognized 15 wines but with the institution of national prohibition, it was decided by the revisers of the National Formulary that red wine and white wine be dropped and with them all of the medicated wines made from them. Of these, four now survive in distinctly modified form and bearing other names. These four are *tinctures of antimony* (p. 255) and *ipecac* (p. 255); *stronger tincture of colchicum corm* (p. 255); and *elixir of beef and iron* (p. 229).

OLEORESINS

The pharmaceutic oleoresins are liquid preparations of drugs, containing volatile oil and resin, obtained by percolation of such drug with acetone, ether, or alcohol, and subsequent distillation of the solvent from the dissolved oleoresins.

There are two classes of oleoresins—the *natural oleoresins* and the *pharmaceutic oleoresins.* The former are mixtures of volatile oil and resin exuding from plants, and, as example of these, may be cited the drugs turpentine and copaiba, which are discussed in Chapter XLVII. These are quite different from the pharmaceutic oleoresins defined above as being made by percolation with the appropriate solvent.

It is self-evident that we can prepare pharmaceutic oleoresins only from such drugs as contain volatile oil and resin; that such preparations as "oleoresin of cinchona" and "oleoresin of gentian" are impossible, since neither drug contains oil and resin in appreciable quantities. As drugs containing oil and resin are not very abundant, the number of oleoresins is limited, only two being official.

Manufacture.—The pharmaceutic oleoresins are manufactured by placing the drug *without moistening* in a suitable apparatus, and percolating with the appropriate solvent. When the solvent is distilled from the percolate, there is a small quantity of oily liquid left behind, and this constitutes the official oleoresin.

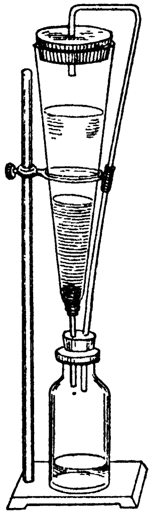


Fig. 190.—Volatile liquid percolator.

If the menstruum used in percolation is alcohol, the extraction is carried on in an ordinary percolator; but if the solvent is acetone or ether, extraction in an ordinary percolator is both wasteful and dangerous, by reason of the inflammability of the solvent.

In such cases, percolation must be conducted in apparatus so arranged to reduce evaporation to the minimum. Such a percolator is pictured in Fig. 190. Of course, both percolator and receiving bottle cannot be tightly corked, else the dropping of the liquid would be impossible. Accordingly, the corks closing the tops of the percolator and receiving bottle are pierced by glass tubes drawn to tapering points, through which the air may pass without very great evaporation of the ether.

It is found convenient to connect these glass tubes with a rubber tube, although some sticklers disapprove of the use of the rubber tubing by reason of the contamination, through possible solution, of a small part of the rubber by the vapors of ether as they pass through.

Strength.—The strength of oleoresins is uncertain, inasmuch as different samples of the same drug may contain entirely different amounts of their oleoresinous constituent. The oleoresins, however, represent the most concentrated form of liquid pharmaceuticals, being usually from five to ten times stronger than the drug.

TABLE OF OFFICIAL OLEORESINS

Solvent	
Ether	Oleoresin of aspidium.
	Oleoresin of capsicum. N.F. VI.
	Oleoresin of ginger. U.S.P. IX; N.F. VI
Alcohol	Oleoresin of cubeb. U.S.P. IX; N.F. VI.

SPECIAL NOTES ON OFFICIAL OLEORESINS

OLEORESINA ASPIDII—Oleoresin of Male Fern

(Oleores. Aspid.—Oleoresin of Male Fern)

Oleoresin of Aspidium yields not less than 24 per cent of crude filicin.

Storage.—Preserve oleoresin of aspidium in well-closed containers.

Condensed Recipe.

Freshly ground aspidium (500 Gm.) in No. 20 powder is exhausted by percolation with ether in a volatile liquid percolator. Most of the ether is recovered from the percolator by distillation and residue is freed from the rest of the ether by spontaneous evaporation. For details see U.S.P., p. 246.

Remarks.—The precipitate that forms in this oleoresin consists of the valuable constituent, filicin, and this oleoresin must, therefore, be dispensed with a "shake" label.

Note that the drug used must be freshly ground and that filicin assay is provided.

Dose.—4 Gm. (60 grains). *Caution.*—Give single dose once a day.

Oleoresina Capsici (U.S.P. X; N.F. VI) or *Oleoresin of Capsicum* is prepared by exhausting capsicum, in No. 20 powder, by percolation with ether. The procedure is exactly as in making oleoresin of aspidium, except that at the end of the operation the liquid oleoresin is separated from the fatty matter by decantation, or by draining through cotton. The fatty matter is rejected. For details see N.F., p. 266. An "organoleptic" assay for this oleoresin is provided; based upon the persistence of pungency even in a highly diluted, sweetened aqueous solution of the oleoresin. The oleoresin of capsicum is used in the preparation of capsicum plaster. *Dose.*—0.015 Gm. (¼ grain).

Oleoresina Cubebæ (U.S.P. IX; N.F. VI) or *Oleoresin of Cubeb* is made by percolation of cubeb with alcohol, with recovery of the solvent by distillation. Note that this oleoresin is made with alcohol as the menstruum; not with ether as commonly obtains. Note that the waxy precipitate is to be rejected, since it is inert and not valuable, as is the precipitate in oleoresin of aspidium. *Dose.*—0.5 Gm. (8 grains).

Oleoresina Lupulini (N.F. IV) is prepared by percolating lupulin with ether. In U.S.P. VIII acetone was used as the menstruum. *Dose.*—0.2 cc. (3 grains).

Oleoresina Petroselini (U.S.P. IX) or *Oleoresin of Parsley Fruit* is made like oleoresin of aspidium except the clear liquid oleoresin is decanted from the solid residue after five days of sedimentation. This preparation is commonly called apiol although it is not the true chemical bearing the name. (See p. 820.) It is used as an emmenagogue and that so frequently illegitimately that in some states its sale is prohibited except upon a physician's prescription. *Dose.*—0.5 cc. (8 minims).

Oleoresina Piperis (U.S.P. IX) or *Oleoresin of Pepper*, is made by percolating black pepper with ether; the procedure being exactly as in making oleoresin of capsicum; the filtration through cotton being designed to remove the piperin. After the ether has mostly evaporated, the piperin begins to crystallize from the liquid, and U.S.P. IX directed that these crystals of piperin be removed from the oleoresin by straining through cotton. This oleoresin is prescribed in the South as *oil of black pepper*. *Dose.*—0.03 Gm. (½ grain).

Oleoresina Zingiberis (U.S.P. IX; N.F. VI) or *Oleoresin of Ginger* is made like oleoresin of aspidium, except that the drug is to be in a No. 60 powder and not necessarily freshly ground. *Dose.*—0.03 Gm. (½ grain).

VINEGARS

Vinegars are liquid preparations obtained by extracting the active principle of drugs by maceration or percolation with vinegar or with diluted acetic acid.

This is one of the oldest classes of liquid medicinal preparations, and resembles tinctures in everything but the solvent employed. Diluted acetic acid, or its impure form—vinegar—is an excellent solvent for the active principles of many drugs, and is a preservative as well; hence the ancient uses of medicated vinegars and the former employment of 10 per cent acetic acid as menstruum in some fluidextracts (p. 263).

However, the vinegars themselves have been largely supplanted by tinctures and fluidextracts, there now being but one—*vinegar of squill*—retained in the Pharmacopœia. There are none in the National Formulary.

ACETUM SCILLÆ—Vinegar of Squill

(Acet. Scil.)

Condensed Recipe.

Squill, in No. 20 powder (100 Gm.), is macerated seven days with diluted acetic acid. The mixture is strained and the strainer washed with enough of the acid to make 1 liter. The strained liquid is heated to boiling, is filtered while hot and finally enough diluted acetic acid is added to make 1 liter. For details see U.S.P., p. 12.

Remarks.—In preparing this preparation, the straining, boiling and filtering is to coagulate and to remove the albumin extracted from the drug.

Since the present official vinegar of squill has been boiled, the official *syrup of squill* prepared from it can be made without boiling of vinegar, directed by the Pharmacopœia of 1890.

Dose.—1 cc. (15 minims).

Acetum Aromaticum (N.F. V) is made by dissolving oils of lavender, rosemary, juniper, peppermint, cinnamon, lemon and clove in alcohol and then adding to the solution acetic acid and water. The alcohol content is about 25 per cent.

Acetum Opii (N.F. IV) is made by macerating opium, myristica and sugar in diluted acetic acid for seven days after which it is to be filtered by percolation. U.S.P. VIII directed that the opium and myristica be macerated and expressed by successive treatment with two portions of diluted acetic acid (500 and 200 cc. each). After filtration, sugar was dissolved in the expressed liquids and enough of the menstruum added to make the finished product represent 10 per cent of opium. The preparation is known as *black drop*; a dangerous synonym since more than once it has been dispensed with fatal results on prescriptions calling for *black draught* (compound infusion of senna).

BIBLIOGRAPHY

Fluidextracts.—(History) Hodgson, A.J.P., 2, 1831, 285; Ellis, A.J.P., 6, 1835, 274, (Manufacture) Lloyd, A.Ph.A., 35, 1887, 582; Allaire, A.Ph.A., 23, 1875, 62. (Repercolation) Squibb, A.Ph.A., 13, 1865, 201; *ibid.*, 14, 1866, 81; *ibid.*, 15, 1867, 391; *ibid.*, 18, 1870, 181; *ibid.*, 26, 1878, 708; Arny and Oxley, A.Ph.A., 58, 1910, 1104; Kelly and Krantz, Jl. A.Ph.A., 13, 1924, 815. (Preservation) Scoville, A.Ph.A., 58, 1910, 874. (Precipitation) Lloyd, A.J.P., 80, 1908, 39; Javillier and Guerithault, Bull. sci. pharmacol., 18, 1911, 937. Scoville, Jl. A.Ph.A., 8, 1919, 799.

Fluidextract of Ergot.—Wokes and Elphick, Quart. J. Pharm., 2, 1929, 539; Breddin, Ph.Zt., 75, 1930, 336.

Fluidextract of Hydrastis.—Albanese and Pedroni, C.A., 23, 1929, 666.

Fluidextract of Senega.—Kennedy, A.Ph.A., 27, 1879, 721.

Aromatic Fluidextract of Cascara.—Grazer, Pharm. Rund., 6, 1888, 9; Anon., West. Dr., 12, 1890, 378; Edel, West. Dr., 17, 1895, 281, and 18, 1896, 391; Harris and Davy, Jl. A.Ph.A., 19, 1930, 28.

Fluidextract of Senna.—Siebold, Ph. Jl., [3], 6, 1875, 445 and 456; Ellis, A.J.P., 6, 1834, 274.

Fluidextract of Gentian.—Bartlett, Jl. A.Ph.A., 13, 1924, 27.

Fluidextract of Glycyrrhiza.—Scoville, Jl. A.Ph.A., 10, 1921, 688; Berg, Jl. A.Ph.A., 13, 1924, 814.

Acetic Fluidextracts.—Wulling, A.Ph.A., 47, 1899, 427; Squibb, A.Ph.A., 49, 1901, 570.

Fluid Glycerates.—Beringer, A.Ph.A., 56, 1908, 981.

Wines.—(Manufacture) Virey, Jl. Ph. et Ch., 1, 1823, 417.

Oleoresins.—(History) DuMez, Univ. Wisc. Bull., 1919, No. 980. (Manufacture) Procter, A.J.P., 18, 1846, 167; *ibid.*, A.J.P., 21, 1849, 114; Maisch, A.J.P., 44, 1872, 208; Beringer, A.J.P., 64, 1892, 145. (Cubeb) Procter, A.J.P., 38, 1866, 210; *ibid.*, 18, 1846, 169. (Male fern) Greenawalt, A.J.P., 61, 1889, 169. DuMez, Phillip, Jl. Sci., through C.A., 9, 1915, 2288; Csipke, C.A., 23, 1929, 4769.

Vinegars.—(Manufacture) Virey, Jl. de. Ph., et Ch., 1, 1823, 433. (Black drop) Virey (see above); Anon., A.J.P., 29, 1851, 187; Anon., Ph. Jl., 16, 1856, 246. (Squill) Virey (see above).

CHAPTER XVI

OFFICIAL LIQUIDS CONTAINING UNDISSOLVED MATTER

MIXTURES

MIXTURES are aqueous preparations for internal use containing insoluble nonfatty substances. Since they contain insoluble matter, they must be dispensed with a "Shake Well!" label. They differ from emulsions in containing no fat; from liniments, in being used internally.

Up to the revision of 1890 both mixtures and emulsions were grouped under the common head Mistura, but at that revision the class *emulsions* was given pharmacopœial recognition.

As mixtures usually contain some organic matter, with water as a vehicle, they are prone to fermentation, and are accordingly unstable. A possible exception to this rule is the compound mixture of opium and glycyrrhiza; but even this popular remedy should not be made in too large a quantity.

In prescriptions calling for insoluble substances in an aqueous vehicle it is frequently considered good pharmacy to prepare a *suspension* by the use of some mucilaginous material. Bateson recommends for this purpose, compound powder of tragacanth of the British Pharmacopœia. This is made by mixing 15 Gm. of tragacanth, 20 Gm. of acacia, 20 Gm. of starch, and 45 Gm. of sugar.

TABLE OF OFFICIAL MIXTURES

Process	*Galenic preparations*	*Chemical preparations*
All by simple admixture.	Carminative mixture (N.F. VI).	Compound iron mixture, U.S.P. VIII.
	Chalk mixture.	
	Expectorant mixture (N.F. VI).	
	Mixture of copaiba (N.F. VI).	
	Mixture of opium and glycyrrhiza, compound.	
	Mixture of rhubarb, compound (U.S.P. VIII; N.F. VI).	

SPECIAL NOTES ON OFFICIAL MIXTURES

MISTURA CRETÆ—Chalk Mixture

(Mist. Cret.)

Condensed Recipe.

Ingredients.—Compound chalk powder, 20 Gm.; cinnamon water, 40 cc.; distilled water, enough to make 100 cc.

Manipulation.—Triturate the powder with the cinnamon water and about 20 cc. of distilled water; transfer to a graduated vessel rinsing the mortar with distilled water. For details see U.S.P., p. 236.

Remarks.—The recipe for this old diarrhea remedy was changed in the U.S.P. X. Prepared chalk and glycerin taking place of the chalk acacia and sucrose. The U.S.P. XI however returns to the old formula. The objection to the present formula is that fermentation occurs when it is kept any length of time. For this reason the U.S.P. directs that it must be dispensed only when recently prepared.

Dose.—15 cc. (4 fluidrachms).

MISTURA OPII ET GLYCYRRHIZÆ COMPOSITA—Compound Mixture of Opium and Glycyrrhiza

(Mist. Opii et Glycyrrh. Comp.—Mistura Glycyrrhiza Composita U.S.P. X, Compound Mixture of Glycyrrhiza, Brown Mixture)

Condensed Recipe.

Ingredients.—Fluidextract of glycyrrhiza, 120 cc.; antimony and potassium tartrate, 0.240 Gm.; camphorated tincture of opium, 120 cc.; spirit of ethyl nitrite, 30 cc.; glycerin, 120 cc.; distilled water, enough to make 1000 cc.

Manipulation.—Mix the fluidextract, and the glycerin with 500 cc. of distilled water; add the tartar emetic dissolved in hot water; then add the other ingredients and enough water to make 1 liter. For details see U.S.P., p. 236.

Alcohol content 9 to 11 per cent by volume.

Remarks.—This mixture, called *brown mixture,* by reason of its color, is often prescribed in the South under the Latin name "Mistura Fusca" —the latter word being Latin for brown. In the present Pharmacopœia the title has been changed to include opium because of the policy of designating therapeutically active ingredients in the title. Brown mixture is used as a simple remedy in coughs, and for this purpose it is quite efficient.

Dose.—4 cc. (1 fluidrachm).

Mistura Ferri Composita (N.F. IV) is commonly called *Griffith's mixture.* It contains ferrous carbonate produced by the chemical reaction between ferrous sulfate and potassium carbonate; hence it can best be considered under iron salts in Part III.

Mistura Rhei Composita (U.S.P. VIII; N.F. VI) previously recognized in the National Formulary under the name, *mistura rhei et soda* and still popularly called for under the name of rhubarb and soda mixture is made from the fluidextracts of rhubarb and ipecac, sodium bicarbonate, and spirit of peppermint, diluted with glycerin and water and is used in some sections as a remedy for flatulence. It does not, however, enjoy universal popularity being rarely prescribed in the South. The National Formulary V also contained a recipe for an alkaline mixture of rhubarb which has been deleted in the new edition. *Dose.*—4 cc. (1 fluidrachm).

DOSES OF OFFICIAL MIXTURES

0.5 cc. (8 minims) for infants....	Carminative mixture (N.F. VI).
4 cc. (1 fluidrachm)............	Compound mixture of opium and glycyrrhiza. Compound mixture of rhubarb (N.F. VI). Expectorant mixture (N.F. VI).
8 cc. (2 fluidrachms)............	Mixture of copaiba (N.F. VI).
15 cc. (4 fluidrachms)...........	Chalk mixture.

MIXTURES OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amounts used in 1000 cc)	Remarks.
Mistura carminativa.	Dalby's carminative.	Magnesium carbonate, 65 Gm ; potassium carbonate, 3 Gm.; tincture of opium, 25 cc.; oils of caraway, fennel and peppermint; syrup; distilled water.	*Dose.*—(For infants) 0.5 cc. (8 minims).
Mistura copaibæ.	Lafayette mixture.	Copaiba, 125 cc.; sodium nitrite; compound tincture of lavender; solution of potassium hydroxide syrup, acacia, distilled water.	*Dose.*—8 cc. (2 fluidrachms).
Mistura pectoralis.	Stokes' expectorant.	Ammonium carbonate; fluidextracts of senega and squill; camphorated tincture of opium, 175 cc.; distilled water; syrup of tolu balsam.	*Dose.*—4 cc. (1 fluidrachm).
Mistura rhei composita.	Mixture of rhubarb and soda.	Fluidextracts of rhubarb and ipecac; sodium bicarbonate; spirit of peppermint; glycerin; distilled water.	*Dose*—4 cc. (1 fluidrachm).

LOTIONS

Lotions are fluid preparations, usually containing suspended insoluble matter and applied externally. They differ from mixtures in being designed for external use and from liniments in being aqueous, rather than oleaginous or alcoholic. No lotions are recognized in the Pharmacopœia but the following are given place in the National Formulary.

Lotio Alba (N.F. VI) also called *white lotion* and *Lotio Sulfurata* is made by dissolving zinc sulfate and sulfurated potash separately in distilled water, filtering and slowly adding the sulfurated potash solution to the zinc sulfate solution with constant stirring and bringing the volume up to required amount with distilled water. It should be made up freshly as required and shaken thoroughly before dispensing. *Lotio Alba Veterinaria* (N.F. V) or *veterinary white lotion* is made from zinc sulfate, lead acetate, and water.

Lotio Ammoniacalis Camphorata (N.F. V) is called *sedative water* or *eau sedative de Raspail.* It is made by dissolving sodium chloride in water and adding thereto spirit of camphor and ammonia water. It enjoys considerable popularity in the South as a headache lotion.

Lotio Calaminæ (N.F. VI) is made by trituration of prepared calamine and zinc oxide with glycerin and lime water.

Lotio Calaminæ Phenolata (N.F. VI) is the foregoing with 10 cc. of liquefied phenol to the liter.

Lotio Flava (N.F. VI) and **Lotio Nigra** (N.F. VI) will be discussed under the mercurial preparations (Chapter XXXIV).

Lotio Plumbi et Opii (N.F. VI) the well-known *lead and opium wash* is made from lead acetate, tincture of opium and distilled water. (See p. 607.)

JULEPS AND LOOCHES

Juleps are pleasantly flavored, mucilaginous preparations enjoying some popularity as vehicles in England and in France. A typical julep is the *mistura gummosa* of the earlier German and French Pharmacopœias. This is prepared by triturating 10 parts of acacia with 30 parts of syrup of acacia, 100 parts of water, and 10 parts of orange flower water. Similar to juleps are the *looches.* Looch blanc or *white linctus* is a type of emulsion of almond.

GARGLES

Gargarismæ or gargles are aqueous preparations containing medicaments intended to relieve throat troubles. The method of application is indicated by the name.

Gargarisma Potassii Chloratis cum Ferro (N.F. VI) also known as *golden gargle* or *gargle of potassium chlorate with iron* is the only gargle listed in the official standards and is made by dissolving potassium chlorate in a mixture of glycerin and distilled water and adding tincture of ferric chloride. The National Formulary V gave a recipe for **Gargarisma Guaiaci Compositum** which contains ammoniated tincture of guaiac, compound tincture of cinchona, honey, potassium chlorate (40 Gm. to the liter) oil of peppermint and water. From this it is seen that gargles are not necessarily clear fluids.

EMULSIONS

Emulsions are aqueous preparations for internal use in which resinous or fatty substances are suspended by means of mucilaginous matter. Like mixtures, they must be shaken before administration. A typical emulsion is milk, in which the fat (butter) is emulsified by an albuminous substance, casein. Milk is a natural emulsion.

According to the latest ideas of emulsification as advanced by the physical chemists, emulsions are considered to be fine distributions of one liquid in another. The liquid which is dispersed or distributed in fine globules is called the *internal* or *disperse* phase, and the liquid in which the fine globules are suspended is called the *dispersion medium* or *external phase*. There are two types of emulsions used in pharmacy, the oil-in-water type and the water-in-oil type. Almost all emulsions which are intended for internal use, such as cod liver oil, chloroform, etc., belong to the first type, where the oil droplets coated with a film of hydrated mucilaginous colloid are suspended in water. The film around the droplets prevents their running together. This hydrated colloid theory is not universally adopted, thus Briggs and his coworkers believe the presence of finely divided solids is the *sine qua non* of emulsions made by the Continental method. The best "finely divided solids," that is, the best emulsifiers, are those readily wetted by the external phase. Nuttall agrees with this finding, stating that there is a direct connection between wetting, frothing, and emulsifying power. Preparations like hydrous wool fat, intended for external use are emulsions of the water-in-oil type, in which water is suspended in the form of droplets. Roon points out that such pharmaceuticals as cold cream, mercurial ointment, ointment of mercuric nitrate, ammonia liniment and lime liniment are emulsions, even though they are not so called. Nuttall states that froth and foam are emulsions of air in water.

During the past decade much has been written as to the physics of emulsions. At the risk of being considered heterodox, the present writer dares to express his opinion that most of the theories presented are old pharmaceutic truths expressed in the modern jargon of physical chemistry. Many of the papers discuss soap emulsions and other types of more importance in general technology than in pharmacy. A number of typical papers are given in the bibliography at the end of this chapter and of these the only one, in our opinion, having a direct bearing on dispensing pharmacy is the one by Smith and his coworkers. Smith's findings may be summarized as follows: (*a*) the finer the subdivision of the oil globules the more stable the emulsion; (*b*) separation of the "cream" from an emulsion can be explained by Stokes' law; (*c*) to minimize "creaming" we must either decrease the difference in density between the oil and the aqueous phase or decrease the size of the oil globules; (*d*) acacia is the safest emulsifier for edible emulsions; (*e*) other gums, notably tragacanth or chondrus may be added to increase the viscosity of the emulsion and thus to delay "creaming."

Emulsions, like mixtures, are rather unstable, and should be freshly prepared when desired. This question of freshness may be extended to the statement that no emulsion more than a week old should be dispensed. The proprietary emulsions which are marketed quite largely are invariably made stable by adding preservatives, the most innocent of which are glycerin or alcohol.

In making emulsions, druggists have the opportunity of exhibiting the highest degree of pharmaceutic art, and there is no reason why the pharmacist should not make all the emulsions he dispenses, except, of course, those proprietary brands specified by the prescriber. Reserving the discussion of the official emulsions until later, we will first consider the important processes of emulsification.

The emulsion of cod liver oil is the best illustration of an emulsion of a fixed oil. It is manufactured by two methods—the English method and the Continental method—and of these, the simplest method of manufacturing is by the Continental method. The secret of the successful manipulation by the Continental method consists in wisely choosing the proportions of gum, water, and oil employed, these proportions being: oil, 4 parts; water, 2 parts; and gum, 1 part; or, to express it in other words, use twice as much water as gum, and twice as much oil as water. The manipulation is fully explained on pages 288 and 289 and consists of triturating the gum with the oil, adding the water all at once, and stirring rapidly until the emulsion results. The emulsion nucleus, as it is called, can be easily diluted with water, syrup, and flavors to the required quantity, it being the general custom in this country to dispense the emulsion of cod liver oil containing 50 per cent of oil. The objection to the 50 per cent acacia emulsion is that the resulting product is quite thick and difficult to pour out from a bottle; and, moreover, the use of a large quantity of gum arabic required makes the emulsion rather expensive. For this reason, other gums have been used besides gum arabic, such as tragacanth, Irish moss, gelatin, and dextrin.

Powdered gelatin has also been used in the manufacture of emulsions, and when a combination of powdered gelatin and tragacanth is used, the emulsion can be made in a bottle without the use of a mortar. Powders for the manufacture of these so-called "flask emulsions" were exploited some years since, and the best known of them, when examined by the author, was found to consist of saponin, saccharin, and a small quantity of a gummy substance. As neither saponin nor saccharin should be used indiscriminately, it is hardly necessary to state that the pharmacist should be chary in employing such substances in emulsions.

Of late, soap is being used as an emulsifier, Scoville finding that 0.15 Gm. of sodium oleate and 3 cc. of water will emulsify 97 cc. of olive oil, the resulting emulsion being a jelly. Since so small a quantity of soap is required, a 50 per cent emulsion is free from soapy taste and is more fluid than are gum emulsions.

Scoville has found on the market a 35 per cent emulsion of cod liver oil containing sodium silicate as emulsifier. He suggests the following recipe for this sort of preparation: oil, 40 cc.; solution of sodium silicate, 2 cc.; crystalline aluminum sulfate, 0.9 Gm.; water and flavor to make 100 cc.

If an emulsion of castor oil is required, it is made like emulsion of cod liver oil, and the recipe for the same can be found in the National Formulary.

In making emulsions of fixed oils according to the English method, the process consists of triturating gum with water, thus making a mucilage, and adding a small quantity of oil, then adding a little water, and then a little oil, and so on, adding the oil and water alternately until the emulsions are completed. This method of manufacturing the emulsions is slow and uncertain, and cannot be compared in simplicity with the preparation of emulsions by the Continental method. It has, however, the advantage that the comparatively large amount of oil can be emulsified by the addition of a small quantity of gum; and when a physician, therefore, prescribes an emulsion containing less gum than is required by the method of manufacturing according to the Continental method, the English method of emulsification is indicated.

Very frequently the manufacture of emulsion results in a failure, and the product, instead of being a creamy-white product, is an ugly, greasy mixture. This failure in making emulsions is what is called "splitting" an emulsion. Such a split emulsion can be redeemed by adding it gradually to a concentrated perfect emulsion, following the dictum that "the best emulsifier is a perfect emulsion."

Emulsions of volatile oils can be prepared either with gum arabic or tragacanth, although the latter, in the hands of the author, gives more satisfactory results. The manufacture of a typical emulsion of a volatile oil is found in the process given for making emulsion of turpentine (U.S.P.), in which recipe acacia is used as the emulsifier. The recipe can be used for any other volatile oil by substituting such volatile oil for the oil of turpentine in the official recipe.

La Wall has found on the market a volatile oil emulsion in which the emulsifying agent was a mixture of 20 per cent of powdered egg albumin and 80 per cent of potassium bitartrate. His experiments indicated that 1 Gm. of this emulsifier was sufficient to prepare 200 cc. of a 50 per cent emulsion of a volatile oil that was heavier than water. For specifically light volatile oils, 2½ times of the above amount of emulsifier was found necessary.

By use of a colloid mill, Whitmore and Linehan prepare 5 per cent transparent emulsions of volatile oils, using 0.25 per cent of gelatin as the peptizing (p. 951) agent and a mixture of 2 parts of invert sugar and 1 part of sucrose to prevent graining.

In all emulsions that we have thus far considered the emulsifying agent is a gummy substance. Such emulsions have decided limitations, however, the gum being thrown out of the combination by the addition of alcohol, glycerin, or tincture of iron in anything more than in small quantities. For this reason the best emulsifying agent is yolk of egg, and the recipe for emulsion of cod liver oil made with a yolk of egg as a base is found in the National Formulary. Another egg emulsion of cod liver oil is one devised by the author, which is found on page 289.

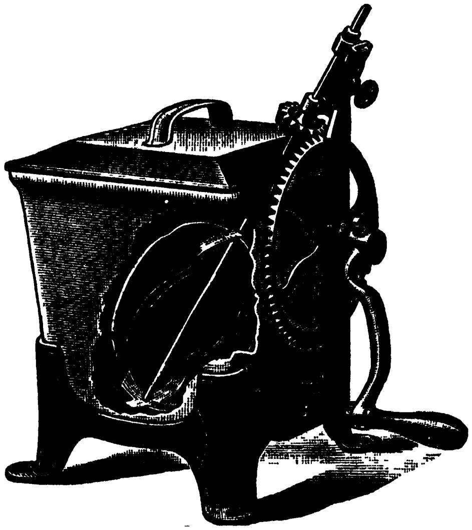


Fig. 191.—Hand emulsion machine.

Extract of malt is also a valuable emulsifying agent; a recipe being given in the National Formulary. Another satisfactory recipe is as follows: Extract of malt, 1 part; triturate with cod liver oil, 4 parts; then add syrup of wild cherry, 2 parts, and sherry wine, 1 part.

Casein has also been suggested as an emulsifying agent, it being the emulsifier in milk. In the writer's hands, however, the commercial casein has never yielded satisfactory results, nor has he been any more fortunate when using condensed milk, which has been suggested as an emulsifying agent.

The *flavor* of an oil emulsion is a matter of importance especially in the case of emulsion of cod liver oil. The general monograph on emulsions given in the National Formulary suggests several flavors. Beringer reports that the best disguisers of the "fishy" taste are oils of coriander, geranium, anise, and cardamom. Smith prefers oils of cinnamon, fennel, and celery.

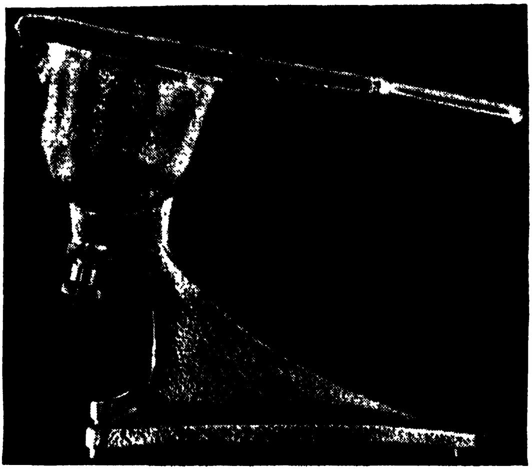


Fig. 191*a*.—Portable hand homogenizer. (Courtesy of International Emulsifiers, Inc.)

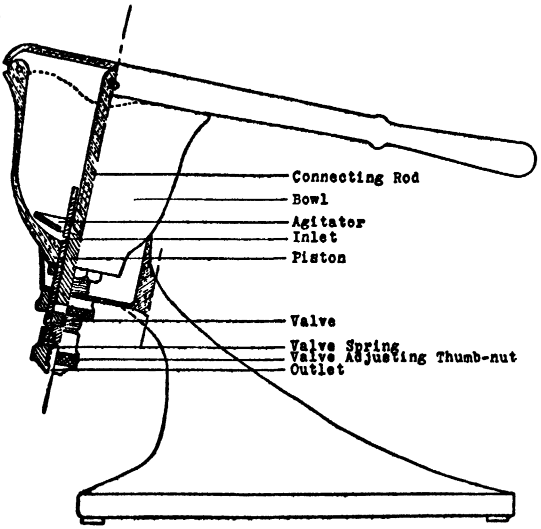


Fig. 191*b*.—Diagram of portable hand homogenizer showing parts. (Courtesy of International Emulsifiers, Inc.)

As to *apparatus*, the mortar and pestle are used for most extemporaneous emulsions, although, as stated on page 289, some emulsions can be made in a bottle. Cox points out that the average fixed oil emulsion may be quickly prepared by placing the mucilage, the oil, and the water in a glass graduate and then vigorously pumping the mixture with an ordinary glass syringe. For large quantities of pharmaceutical emulsions special emulsion machines (Figs. 191*a* and *b* and 192) are available. There are now in the market high power emulsifiers, known as *homogenizers*, used chiefly for making "synthetic" milk or cream. These machines produce an emulsion with surpassingly fine oil globules and they are now being used in manufacturing pharmacy (Fig. 191*a*). A hand homogenizer of moderate price is now available to retail pharmacists (Fig. 191*b*).

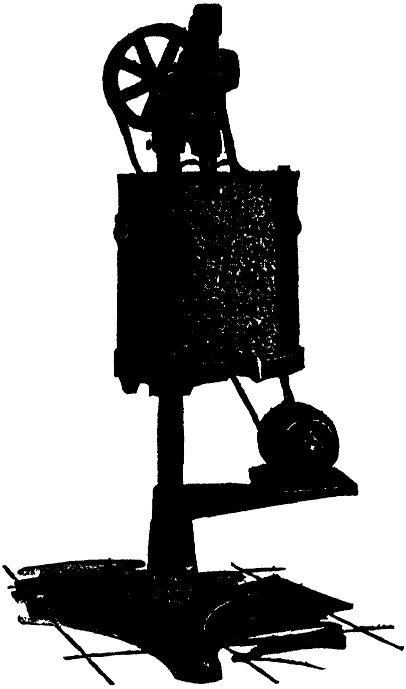


Fig. 192.—Stokes' emulsifier and mixer.

TABLE OF OFFICIAL EMULSIONS

(ALL GALENIC)

In addition to the prepared emulsions listed below the National Formulary VI lists *cow's milk* which is a natural emulsion.

Gum-resin emulsion.....	Emulsion of asafetida.
Fixed oil emulsion.......	Emulsion of cod liver oil.
	Emulsion of cod liver oil with egg (N.F. VI).
	Emulsion of cod liver oil with hypophosphites (N.F. VI).
	Emulsion of cod liver oil with malt (N.F. VI).
	Emulsion of liquid petrolatum.
	Emulsion of liquid petrolatum with phenolphthalein (N.F. VI).
Volatile oil emulsion.....	Emulsion of oil of turpentine.

SPECIAL NOTES ON OFFICIAL EMULSIONS

EMULSUM ASAFŒTIDÆ—Emulsion of Asafetida

(Emuls. Asafœt.—Milk of Asafetida)

Condensed Recipe.

Rub asafetida, in tears (40 Gm.) with distilled water to a smooth emulsion. Strain and wash strainer with enough water to make 1 liter. For details see U.S.P., p. 141.

Remarks.—Asafetida, as explained on page 876, is a gum-resin; it consists of a water-insoluble resin and a water-soluble gum. If we rub asafetida with water, the gum on dissolving, will emulsify the resin, and a milky mixture, familiarly called *milk of asafetida*, results.

In making this emulsion the whole drug asafetida is placed in a mortar and triturated with water until the emulsion results. Under no circumstances should the powdered drug be used, since the preparation owes its activity to volatile oils, and in getting the drug brittle enough to powder it is necessary to dry it by heat, and this results in driving off an appreciable quantity of the oils. In order to make a good emulsion the best quality of asafetida (tears) should be employed.

The exceedingly unpleasant and persistent odor of asafetida has led to methods of preparing the emulsion in some way other than of triturating the drug in a mortar, for removing the odor from the mortar after making the emulsion is a matter of difficulty. Moreover, since emulsion of asafetida should be freshly prepared, it means that each time a small quantity of the emulsion is called for it is necessary to use the mortar, with the result of keeping it in a continuous state of malodorousness. One method in vogue among certain druggists for making this emulsion—by diluting the tincture of asafetida with water—is nothing short of criminal, and under no circumstances should it be followed.

Another method that might be criticised, but one which gives fairly good results, is by preparing a glycerite of asafetida by gently warming the gum-resin with glycerin, and thus obtaining a preparation eight times stronger than the emulsion. In preparing the emulsion from this glycerite 1 drachm of the glycerite is taken and diluted with 7 drachms of water. The chief objection to the manufacture of glycerite of asafetida is the uncertainty that the drachm of the glycerite will contain the full active amount of asafetida required for an ounce of the full-strength finished product.

After all, the only safe way is the official method, and as an illustration of financial advantage of being "faithful in small things" may be cited the case of a pharmacist who built up a large prescription business from comparatively small beginnings by calling the attention of physicians in his city to the fact that he made this emulsion, as well as other Pharmacopœial staples, "just right."

The disagreeable odor clinging to the utensils used in preparing this emulsion may be combated in three ways.

Best of all is it to have a special mortar for asafetida and other evil-smelling drugs. If that is not feasible, the mortar can be freed from odor by igniting a small amount of alcohol (say 1 to 2 fluidrachms) in the mortar, and triturating the burning liquid with pestle until it is burned out. It is needless to say that the pestle handle must be fitted with plaster-of-paris cement and not with shellac (p. 135), for the latter cement would be softened by the heat of burning alcohol and the handle become loose. Moreover, this method must be cautiously employed, as the sudden heat sometimes cracks the mortar. A third method is trituration of powdered mustard and acetic acid within the malodorous mortar.

Dose.—15 mils (4 fluidrachms).

EMULSUM OLEI MORRHUÆ—Emulsion of Cod Liver Oil

(Emuls. Ol. Morrh.)

Condensed Recipe.

Ingredients.—Cod liver oil, 500 cc.; powdered acacia, 125 Gm.; syrup, 100 cc.; methyl salicylate, 4 cc.; distilled water enough to make 1 liter.

Manipulation.—Triturate the acacia with the oil and with 250 cc. of distilled water to an emulsion. Add the methyl salicylate, the syrup and enough water to make 1 liter. If desired, other flavoring can be used instead of methyl salicylate.

Remarks.—The U.S.P. XI permits replacement of acacia by agar, gelatin, tragacanth or mixtures of any of these provided the resulting emulsion is similar in viscosity and appearance to one made with acacia. If the emulsion is to be kept for any length of time 7 per cent of alcohol may be added, replacing an equal volume of water. Whenever alcohol or alcoholic liquids are added to emulsions they should be added in small portions, shaking after each addition. Every detail of manipulation of this valuable preparation will be found below.

Dose.—Adults: 15 cc. (4 fluidrachms). Infants: 8 cc. (2 fluidrachms).

EMULSUM OLEI TEREBINTHINÆ—Emulsion of Oil of Turpentine

(Emuls. Ol. Tereb.)

Condensed Recipe.

Ingredients.—Rectified oil of turpentine, 15 cc.; powdered acacia, 5 Gm.; water enough to make 100 cc.

Manipulation.—Shake the oil with the acacia in a dry bottle, add 10 cc. of water and shake until an emulsion is formed. Add to this enough water to make 100 cc. and shake thoroughly.

Remarks.—This emulsion contains 15 per cent oil of turpentine, and the rectified oil at that.

Dose.—2 cc. (30 minims).

EMULSUM PETROLATI LIQUIDI—Emulsion of Liquid Petrolatum

(Emuls. Petrolat. Liq.—Mineral Oil Emulsion)

Condensed Recipe.

Ingredients.—Liquid petrolatum, 500 cc.; powdered acacia, 125 Gm.; syrup, 100 cc.; vanillin, 0.04 Gm.; alcohol, 60 cc.; distilled water enough to make 1 liter.

Manipulation.—Triturate the acacia with the liquid petrolatum and with 250 cc. of distilled water to make an emulsion. Add the syrup, alcoholic solution of vanillin and distilled water in divided portions, triturating after each addition. Other methods of emulsification may be used and the acacia may be replaced by agar, gelatin, tragacanth or mixtures of these provided an emulsion of the viscosity and appearance of the one prepared by the foregoing formula results.

Remarks.—"Mineral oil" emulsions are very much in demand and the inclusion of this formula in the U.S.P. XI is in response to this demand. Frequently the basic liquid petrolatum emulsion is medicated with phenolphthalein, cascara sagrada, and other drugs. The National Formulary VI recognizes one such emulsion in which agar and phenolphthalein are used.

Dose.—30 cc. (1 fluidounce).

Emulsum Ammoniaci (U.S.P. 1890) is a 4 per cent emulsion of the gum-resin ammoniac made by triturating the drug in the form of tears, with water.

Emulsion Amygdalæ (U.S.P. IX), or *Emulsion of Almond,* is made by beating blanched sweet almonds (60 Gm.) in a mortar with acacia and sugar and then triturating to a smooth mixture with enough water to make 1 liter. While this preparation is ordinarily grouped as a fixed oil emulsion, we make it from sweet almond (seeds), emulsifying the oil existing therein with gum arabic. The proteids of the almond seed also assist in the emulsification. Note that the almonds must be blanched (p. 740). Emulsion of almond is also known as *milk of almonds,* and is used as a pleasant vehicle in medicine, although its use in this country is rather limited.

Emulsum Chloroformi (U.S.P. VIII) is prepared by shaking 40 cc. of chloroform in a flask with 10 Gm. of powdered tragacanth, and then adding 250 cc. of water. After vigorous shaking, 60 cc. of expressed oil of almond are added to the mixture in several portions and when the emulsion is completed enough water is added little by little to make 1000 cc. of finished product. In making this emulsion, tragacanth is the emulsifying agent, the chloroform being assisted to minute subdivision by means of expressed oil of almond, which also aids in making the emulsion permanent. Note that this is one of the so-called "flask emulsions," being made by shaking the ingredients in a bottle, saving the soiling of a mortar. Another flask emulsion is emulsion of oil of turpentine, and it might be added that all emulsions of volatile oils can be so made. Emulsions of fixed oils and of gum-resins, on the other hand, should always be made in a mortar. *Dose.*—8 cc. (2 fluidrachms).

EMULSIONS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients. (figures show amount used in 1000 cc.)	Remarks.
Emulsum olei morrhuæ cum hypophosphitibus.	Emulsion of cod liver oil with hypophosphites.	Cod liver oil, 500 cc.; hypophosphites of calcium, potassium, and sodium; acacia; saccharin; tincture of sweet orange peel; distilled water.	*Dose.*—15 cc. (4 fluidrachms).
Emulsum olei morrhuæ cum malto.	Emulsion of cod liver oil with malt.	Cod liver oil, 300 cc.; tragacanth; distilled water, extract of malt.	See p. 287. *Dose.*—15 cc. (4 fluidrachms).
Emulsum olei morrhuæ cum ovo.	Emulsion of cod liver oil with egg.	Cod liver oil, 500 cc.; syrup; fresh egg yolk; tincture of sweet orange peel; distilled water.	*Dose.*—15 cc. (4 fluidrachms).
Emulsum petrolati liquidi cum phenolphthaleino.	Emulsion of liquid petrolatum with phenolphthalein.	Heavy liquid petrolatum, 500 cc.; agar; acacia; phenolphthalein; alcohol; vanillin; saccharin; distilled water.	*Dose.*—15 cc. (4 fluidrachms). Each dose contains 0.06 Gm. of phenolphthalein.

DOSES OF OFFICIAL EMULSIONS

2 cc. (½ fluidrachm)	Emulsion of oil of turpentine.
8 cc. (2 fluidrachms)	Emulsion of cod liver oil (infants).
15 cc. (4 fluidrachms)	Emulsions of asafetida, cod liver oil (adults), cod liver oil with egg (N.F. VI), cod liver oil with hypophosphites (N.F. VI), cod liver oil with malt (N.F. VI) and liquid petrolatum with phenolphthalein (N.F. VI).
30 cc. (1 fluidounce)	Emulsion of liquid petrolatum.

LABORATORY EXERCISE

MAKE EMULSION OF COD LIVER OIL

(By Continental Method)

Cod liver oil	30 cc.
Water	15 cc.
Powdered acacia	7.5 Gm.
Water, syrup, and flavor, to make	60 cc.

Put the acacia in a dry mortar and add all the oil, triturating the mixture well. Then add the water (15 cc.) all at once and triturate vigorously until a creamy emulsion results. Lastly, add syrup 5 cc., flavor to taste, and add water to make 60 cc.

Remarks.—The theory of emulsions is similar to that of making blue mass and other preparations and free mercury, the oil being broken into fine globules by trituration and each globule immediately coated with a layer of gummy substance, thus preventing adjacent globules from running together.

The two methods of emulsification are called the English and the Continental processes (see p. 281), and the above recipe is by the Continental process, and practically that recognized by the present Pharmacopœia (p. 281).

Note the proportions essential to a successful Continental emulsion: 4, 2, and 1; 4 parts of oil, 2 parts of water, and 1 part of gum.

For flavor, the Pharmacopœia directs 1/10 of 1 per cent of methyl salicylate, oil of gaultheria, or an appropriate quantity of any other flavor may be used. The finished acacia emulsion is almost too thick for practical use and contains too large an amount of acacia.

The *English emulsion* can be made from less gum, the sole advantage the process possesses.

When oil, gum, and water are triturated a few minutes, a white emulsion should result, the desired effect being indicated by a characteristic crackling sound as the mixture is triturated. If this crackling sound is not heard, and if the mixture has a greasy, "pearly" appearance, it means that the oil is not emulsified—that the emulsion is "split."

Do not Throw Away a Split Emulsion.—Make up another batch as a nucleus, and gradually incorporate the split emulsion, when the entire quantity will be emulsified. There is no better emulsifier than a good emulsion.

MAKE FLASK EMULSION OF COD LIVER OIL

Powdered tragacanth	1 Gm.
Gelatin, in No. 80 powder	1 Gm.
Cod liver oil	20 cc.
Water, flavor, etc., to make	40 cc.

Put the powders in a dry Erlenmeyer flask, add the oil and shake, then add 15 cc. water, and shake, when an emulsion results.

Remarks.—This formula was devised by Arny in 1899 to replace a class of flask emulsifiers introduced about that time, and containing the two questionable substances—saponin and saccharin. With the introduction of inexpensive colloid mills, straight gelatin emulsions are now largely employed. (See Tice, A.J.P., 1935.)

MAKE EGG EMULSION OF COD LIVER OIL

Glycerite of yolk of egg (U.S.P. 1890)	10 cc.
Cod liver oil	30 cc.
Syrup	6 cc.
Brandy	10 cc.
Water	4 cc.

Pour the glycerite into mortar, and add the oil little by little, with constant trituration until completely emulsified. Then add the other ingredients in the order named.

Remarks.—This preparation is emulsified by use of yolk of egg, an emulsion of egg fat with the albuminoids. It is an illustration of the dictum, "the best emulsifier is a perfect emulsion."

Be careful to add oil gradually, else the emulsion may split. The addition of the last portions of oil may make the product almost too stiff to work, in which event add a few drops of water, say, 1 cc. *In laboratory work* omit the brandy from this recipe.

The best flavor for this is a compound tincture of cardamom *not colored* with cochineal. One-half cc. suffices with the above quantity.

MAKE EMULSION OF TURPENTINE

Powdered tragacanth	2 Gm.

Put in dry 8-ounce wide-mouthed bottle and add—

Oil of turpentine	16 cc.
Then add water	30 cc. cork and shake.

The finished emulsion can be diluted with water to any strength directed by the physician. It can be flavored as desired.

Remarks.—This is not the recipe provided by the present Pharmacopœia for official emulsion of oil of turpentine, in which acacia is used as the emulsifying agent.

LINIMENTS

Liniments are liquid preparations for external use, applied by friction. Not all official liniments contain insoluble matter, for, as shown in the table of preparations (p. 194), some are clear alcoholic solutions; in fact, only two of the official liniments—ammonia and lime liniments—both in the National Formulary, are opaque. But since some of the rest are alcoholic solutions—such as soap liniment—and some are clear oleaginous solutions—such as camphor liniment—while one is a more or less transparent semisolid mass—turpentine liniment (N.F. VI)—there seems no definite basis of pharmaceutic grouping of liniments, hence they were left under "liquids containing insoluble matter," to be the last class of pharmaceutic liquids to be discussed.

TABLE OF OFFICIAL LINIMENTS

	Basis	*Galenic preparations*	*Chemical preparations*
Alcoholic.	Alcohol.	Camphor and soap liniment. Soft soap liniment. Compound soft soap liniment (N.F. VI).	Solid liniment of soap (N.F. VI).
	Camphor and soap liniment.	Aconite and chloroform liniment (N.F. VI). Chloroform liniment.	
	Fluidextract.	Belladonna liniment (N.F. VI).	
Oleaginous.	Cottonseed oil.	Camphor liniment.	
	Linseed oil.		Lime liniment (N.F. VI).
	Oil of turpentine.	Acetic liniment of turpentine (N.F. VI). Turpentine liniment (N.F. VI).	
	Olive oil.	Calamine liniment (N.F. VI).	
	Sesame oil.		Ammonia liniment (N.F. VI).

SPECIAL NOTES ON OFFICIAL LINIMENTS

LINIMENTUM CAMPHORÆ—Camphor Liniment

(Lin. Camph.—Camphorated Oil)

Camphor Liniment contains, in each 100 Gm., not less than 19 per cent and not more than 21 per cent of camphor.

Caution.—This preparation is not intended for hypodermic use.

Storage.—Preserve in well-closed containers.

Coarsely powdered camphor (200 Gm.) is dissolved in 800 Gm. cotton seed oil that has been heated on a water bath. For details see U.S.P., p. 200.

Remarks.—In preparing this liniment (commonly called *camphorated oil*) the pharmacist should be very careful in choosing a winter-strained cotton seed oil, that is, an oil that has been filtered during the cold weather, and, therefore, is freed from dissolved solid matter. If the so-called "summer-strained oil" is used in making such a liniment, on the first subjection to cold the liniment will become cloudy, and will scarcely reflect credit upon the pharmacist from whom it was bought. Care should also be taken to dispense this preparation in a dry bottle.

While camphorated oil is now used as a stimulant hypodermically, the Pharmacopœia gives special warning that the liniment as described must not be used for this purpose. A camphorated oil for hypodermic use must be carefully sterilized (see *ampullæ camphoræ*, p. 990).

LINIMENTUM CAMPHORÆ ET SAPONIS—Camphor and Soap Liniment

(Lin. Camph. et Sapon.—Linimentum Saponis U.S.P. X, Soap Liniment)

Condensed Recipe.

Ingredients.—Hard soap, 60 Gm.; camphor, 45 Gm.: oil of rosemary, 10 cc.; alcohol 700 cc.; distilled water, enough to make 1 liter.

Manipulation.—Dissolve the camphor and the oil in the alcohol; then add the soap and the distilled water. Shake until the soap is dissolved; let stand; filter. For details, see U.S.P., p. 201.

Storage.—Preserve in well-closed containers.

Remarks.—Soap liniment is the base of chloroform liniment, and is used quite largely for the extemporaneous preparation of a number of liniments. Thus it is used in preparing a liniment of quinine, which, when applied by friction to children, produces the physiologic effects of quinine without the bitter alkaloid being taken in by mouth.

Soap liniment is sometimes called *liquid opodeldoc,* the original being a preparation similar to the official soap liniment, but containing enough soap to render it solid at ordinary temperatures. When the solid opodeldoc is warmed gently, it liquefies. A recipe for *solid opodeldoc* is found in the National Formulary.

LINIMENTUM CHLOROFORMI—Chloroform Liniment

(Lin. Chlorof.)

Chloroform Liniment contains, at 25° C., in each 100 cc., not less than 40 Gm. and not more than 45 Gm. of $CHCl_3$.

Storage.—Preserve in well-closed containers.

Caution.—Chloroform liniment deteriorates with age.

Condensed Recipe.

Three hundred cc. of chloroform are dissolved by agitation in 700 cc. of camphor and soap liniment. For details, see U.S.P., p. 201.

Remarks.—This liniment is made by mixing soap liniment and chloroform, and is one of the most valuable of penetrating liniments. This liniment is now directed to be assayed and must conform to a definite chloroform standard.

LINIMENTUM SAPONIS MOLLIS—Liniment of Soft Soap

(Lin. Sapon. Moll.—Tincture of Green Soap)

Condensed Recipe.

Dissolve 20 cc. of oil of lavender and 650 Gm. of soft soap in 200 cc. of alcohol. Let stand twenty-four hours, filter and wash the filter with enough alcohol to make 1 liter.

Remarks.—This was called *tincture of green soap* in the Pharmacopœia of 1880, and is prepared by dissolving soft soap in alcohol and flavoring with oil of lavender. It is used almost exclusively as an application to the scalp, and is, therefore, the basis of a number of hair tonics.

Linimentum Ammoniæ (U.S.P. IX; N.F. VI) or *Hartshorn Liniment* or *Volatile Liniment* is a saponaceous emulsion and will be discussed in Part IV.

Linimentum Belladonnæ (U.S.P. IX; N.F. VI) or *Belladonna Liniment,* is made by dissolving 50 Gm. camphor in enough fluidextract of belladonna root to make 1 liter.

Linimentum Calcis (U.S.P. X; N.F. VI), *lime liniment* or *Carron oil* is a saponaceous emulsion and will be discussed in Part IV.

Linimentum Terebinthinæ (U.S.P. IX; N.F. VI) or *Kentish Ointment,* is made by dissolving 650 Gm. melted rosin cerate in 350 Gm. oil of turpentine. It is a semisolid mass and should be dispensed in an ointment jar.

Doses of Liniments.—As all liniments are used externally, no doses are given.

LINIMENTS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients. (figures show amount used in 1000 cc.)	Remarks.
Linimentum aconiti et chloroformi.	Liniment of aconite and chloroform.	Fluidextract of aconite, 45 cc.; alcohol; chloroform; soap liniment.	
Linimentum ammoniæ.	Hartshorn liniment.	....	See above.
Linimentum belladonnæ.	Belladonna liniment.	....	See above.
Linimentum calaminæ.	Calamine liniment.	Calamine and zinc oxide, of each 80 Gm.; olive oil; lime water.	
Linimentum calcis.	Carron oil.	Solution of calcium hydroxide and linseed oil; equal parts.	
Linimentum saponis mollis compositum.	Compound liniment of soft soap.	Soft soap; juniper tar; alcohol.	
Linimentum saponis spissum.	Solid opodeldoc.	Monohydrated sodium carbonate 10 Gm.; stearic acid 50 Gm.; camphor; oils of thyme and rosemary; ammonia water; water and alcohol.	
Linimentum terebinthinæ.	Kentish ointment.	Rosin cerate; oil of turpentine.	
Linimentum terebinthinæ aceticum.	Stokes' liniment.	Oil of turpentine, 400 cc ; oil of lemon; acetic acid, fresh egg, rose water.	Also called *linimentum album* and *St. John Long's liniment.*

DENTILINIMENTA

This is a class of preparations introduced into N.F. V at the suggestion of a committee of the national dental association. They are, as the name implies, liniments to be applied to the gums. The National Formulary V recognizes both compound dental liniment of aconite and compound dental liniment of aconite and iodine but the new Formulary includes only the latter.

Dentilinimentum Aconiti Compositum (N.F. V) or *Compound Dental Liniment of Aconite,* made by dissolving 36 Gm. menthol and 13.5 cc. chloroform in enough tincture of aconite to make 100 cc.

Dentilinimentum Aconiti et Iodi Compositum (N.F. VI) or *Compound Dental Liniment of Aconite and Iodine,* made by dissolving iodine (2 Gm.) in chloroform (30 cc.) adding alcohol, fluidextract of aconite and sufficient distilled water to make 100 cc.

SOLUTIONS

This is another class of dental preparations introduced into the National Formulary V but not continued in the N.F. VI. They consist of chloroformic solutions of resinous material used as pulp capping varnish. The two forms given in N.F. V are:

Solutio Mastiches Chloroformica Composita (N.F. V) pulp capping varnish consisting of mastic, balsam of Peru, and chloroform.

Solutio Resinæ Chloroformica (N.F. V) chloroformic solution of rosin, consisting of rosin and chloroform.

LIQUID PETROXOLINS

These are a class of fluid preparations for external use in which the basis is a combination of liquid petrolatum and ammonium oleate.

Petroxolinum Liquidum or liquid petrox (N.F. VI) is made by mixing light liquid petrolatum and oleic acid, adding alcohol and then stronger ammonia water and after saponification is completed by agitation at room temperature, oil of lavender is added as a perfume. From this is prepared directly the **Iodine Petroxolin** (N.F. VI) which is the only official medicated petroxolin included in the present N.F. It contains 10 Gm. of iodine per 100 cc.

The N.F. V gave formulas for *betanaphthol petroxolin* (containing 10 per cent of betanaphthol), *cade petroxolin* (25 per cent oil of cade), *camphorated chloroform petroxolin* (chloroform and camphor, 20 per cent each), *eucalyptol petroxolin* (20 per cent eucalyptol), *guaiacol petroxolin* (20 per cent guaiacol), *ichthyol petroxolin* (10 per cent of sulphonated bitumen, or ichthyol); *iodine petroxolin* (10 per cent of iodine); *diluted iodine petroxolin* (5 per cent iodine); *menthol petroxolin* (10 per cent menthol); *methyl salicylate petroxolin* (20 per cent methyl salicylate); *phenol petroxolin* (5 per cent phenol); *camphorated phenol petroxolin* (phenol, 12½ per cent and camphor, 37½ per cent are liquefied and are then dissolved in liquid petroxolin); *sulfurated petroxolin* (sulfur, 3 per cent, is dissolved in linseed oil and the fluid dissolved in oleic acid and liquid petroxolin) and *compound sulfurated petroxolin* (10 parts of sulfurated petroxolin are diluted to 100 parts, oil of cade, thymol, eucalyptol, oil of turpentine and liquid petroxolin being used in the dilution).

Petroxolinum Spissum (N.F. VI) or solid petrox is made by mixing melted yellow wax with liquid petrolatum and oleic acid on a water bath and transferring to a warm mortar where it is mixed with the stronger ammonia water and alcohol, stirred until cool and flavored with oil of lavender. This is an excellent base for ointments containing balsam of Peru.

INFUSED OILS

Olea Infusa (N.F. V) are a class of oleaginous preparations for external use, made by macerating the drug with alcohol and ammonia water and then digesting the mixture with sesame oil at 60° to 70° C. until the alcohol and the ammonia water have evaporated. They are supposed to represent in each 1000 Gm., the activity of 100 Gm. of drug. The present Formulary omits this class of preparations but the N.F. V gave a general recipe for infused oils, of which the most popular is the *infused oil of hyoscyamus*, which is the basis of the *compound oil of hyoscyamus* (N.F. V) which is largely used in France, as a remedy for earache under the name *baume tranquille*.

SPRAYS—NEBULÆ

These represent a class of preparations, now largely prescribed by throat specialists, and which consist of light liquid petrolatum in which are dissolved various aromatics and other medicaments. The National Formulary gives recipes for *nebula aromatica* (containing phenol, menthol, thymol, camphor, benzoic acid, eucalyptol, oils of cinnamon and clove and methyl salicylate); *nebula ephedrinæ* containing 1 per cent of ephedrine alkaloid with methyl salicylate; *nebula ephedrinæ composita*, 1 per cent, with camphor, menthol, and oil of thyme; and *nebula mentholis composita* (containing menthol, camphor (1 per cent each), methyl salicylate, and eucalyptol). These sprays are employed in atomizers for carrying the medicinal substances into the passages of the throat and lungs.

Nose Drops.—*Collunaria.*—Preparations now made available under the common title of "nose drops" originated in the modern sense with prescriptions for solutions of menthol and thymol in light liquid petrolatum and directed to be dropped into the nose rather than to be sprayed. Aqueous solutions of nasal remedies are not satisfactory unless they are made isotonic. Recently a number of proprietary preparations have been introduced under the general title of "nose drops." In these preparations the medicating agent is exhibited in the form of an emulsion which has certain advantages over the solutions.

BIBLIOGRAPHY

Mixtures.—Bateson, Ph. Jl., 126, 1931, 52.

Brown Mixture.—Duhamel, A.J.P., 11, 1840, 284.

Mixture of Rhubarb and Soda.—McElhenie, A.Ph.A., 57, 1909, 91.

Chalk Mixture.—Hommel, Merck's Rep., 20, 1911, 46; Fantus and Snow, Jl. A.Ph.A., 11, 1922, 798.

Lotio Alba.—Raubenheimer, Jl. A.Ph.A., 3, 1914, 692.

Emulsions.—(History) Anon., Ch. and Dr., 11, 1870, 121; Gregory, A.Ph.A., 24, 1876, 485; Schelenz, Schw., Ap. Zt., 59, 1921, 657. (Manufacture) Arny, Bull. Pharm., 13, 1899, 326; Bourdier, Jl. de ph. et ch., 26, 1907, 207; Rice, Am. Dr., 14, 1885, 64 and 86; Cox, Dr. Circ., 74, June, 1930, 28; Tice, A.J.P., 107, 1935, 158. (Physics) Bancroft, Jl. Phys. Ch., 16, 1912, 177, 345 and 475; Roon, Jl. A.Ph.A., 5, 1916, 496 and 6, 1917, 263; Roon and Oesper, Jl. Ind. Eng. Ch., 9, 1917, 156; Crockett and Oesper, Jl. Ind. Eng. Ch., 9, 1917, 967; Clayton, Jl. Soc. Ch. Ind., 38, 1919, 113T; Nuttall, Jl. Soc. Ch. Ind., 39, 1920, 67T; Briggs, Du Cassé and Clark, Jl. Phys. Ch., through C.A., 14, 1920, 1474; Thomas, Jl. Ind. Eng. Ch., 12, 1920, 177; Harkins and Keith, Science, 59, 1924, 463; Berry, Ph. Jl., 112, 1924, 664; Kermack, Jl. Soc. Ch. Ind., 44, 1925, 401; Bragg, *ibid.*, 44, 1925, 70; Clayton, *ibid.*, 45, 1926, 288T; Krantz and coworkers, Jl. A.Ph.A., 15, 1926, 83; *ibid.*, 18, 1929,

463, 469, and 797; C.A., 23, 1929, 3388; Jl. A.Ph.A., 19, 1930, 1181; Kyser and Vilbrandt, Jl. A.Ph.A., 14, 1925, 392; Iselin, Ph. Acta Helv., 1, 1926, 45 and 81; Boll. chim. farm., 67, 1928, 225; Harkins and Beeman, Jl. Am. Ch. Soc., 51, 1929, 1674; Smith and coworkers, Quart. J. Pharm., 3, 1930, 354 and 362; Serralach and Jones, Jl. Ind. Eng. Ch., 23, 1931, 1016. (Preservation) Dunning, A.Ph.A., 57, 1909, 70. (Emulsifiers) Painter, A.Ph.A., 35, 1887, 578; Lager, Am. Dr., 16, 1887, 108; Scoville, Bull. Pharm., 29, 1915, 141 and Jl. A.Ph.A., 17, 1928, 1119; Anon., A.J.P., 106, 1934, 406. (Flavors) Beringer, A.J.P., 87, 1915, 115; Smith, Jl. A.Ph.A., 17, 1928, 1174.

Colloid Mills.—McLean, Jl. Ind. Eng. Ch., 16, 1924, 494 and Ch. Met. Eng., 30, 1924, 675; Tice, A.J.P., 107, 1935, 158.

Volatile Oil Emulsions.—La Wall, Jl. A.Ph.A., 14, 1925, 703; Whitmore and Linehan, Jl. Ind. Eng. Ch., 21, 1929, 878.

Emulsion of Cod Liver Oil.—Procter, A.J.P., 45, 1873, 43; Diehl, A.J.P., 54, 1882, 180; Brandup, A.J.P., 106, 1934, 396.

Emulsion of Oil of Turpentine.—Forbes, A.J.P., 44, 1872, 61.

Liniments.—Raubenheimer, A.Ph.A., 58, 1910, 1226.

Opodeldoc.—Rice, Am. Dr., 16, 1887, 22; Buchner, Rep. f.d. Ph., 12, 1822, 249.

Baume Tranquille.—Prado, C.A., 24, 1930, 4898.

CHAPTER XVII

EXTRACTS, ABSTRACTS, RESINS

These three classes of preparations include the only solid pharmaceuticals prepared by percolation.

EXTRACTS

Extracts are solid or semisolid preparations of the soluble and active principles of drugs prepared by percolation of the drug with the appropriate menstruum and evaporation of the percolate.

The menstruum employed varies as much as that directed for fluidextracts, being alcoholic, hydro-alcoholic, aqueous, alcoholic and alkaline, or alcoholic and acid.

A special form of extracts called *inspissated juices*, are popular in England, but have no representative in the present Pharmacopœia of the United States. They were, however, represented in the Pharmacopœia of 1880 by the then official extract of taraxacum. The present official extract of taraxacum is not an inspissated juice, but is prepared by percolation of the drug with hydro-alcoholic menstruum. Extract of taraxacum (U.S.P. 1890) was scarcely a fair type of the inspissated juices, the most prominent of these being the dried juices from the leaves of plants, and, therefore, containing chlorophyl. Such inspissated juices are prepared by bruising fresh leaves or herbs in a stone mortar, pouring off the greenish liquid, and allowing it to stand overnight. The liquid is then strained through calico, thereby separating the chlorophyl; the strained liquid is heated to 200° F., which coagulates the albumin present, and this is removed by straining. The clear liquid is then evaporated to a thin extract, to which is added the chlorophyl, and the whole mixture is evaporated until it is of pilular consistence. Were the plant juices evaporated to extract direct upon expression from the plant, the delicate chlorophyl would be quickly decomposed and a brown extract would result. By first removing the chlorophyl and evaporating the mixture to a thin extract, the chlorophyl is preserved. When added just as the extract is reaching pilular consistence, it has the effect of giving to it an agreeable green color.

Such inspissated juices, as of aconite, belladonna, and hyoscyamus, are very popular in England, but are scarcely used in this country, and it should be borne in mind that these English "extracts" are much weaker than are the official American extracts.

TABLE OF OFFICIAL EXTRACTS
(ALL GALENIC)

Process.	Preparation.	Consistence.
Percolation with evaporation:		
Menstruum, alcohol, U.S.P.	Extract of belladonna.	Powdered.
	Extract of cannabis.	Soft.
	Extract of gelsemium (N.F. VI).	Powdered.
	Extract of hydrastis (N.F. VI).	Powdered.
	Extract of hyoscyamus.	Powdered.
	Extract of stramonium.	Powdered.
Alcohol, U.S.P.; extract defatted	Extract of digitalis (N.F. VI).	Powdered.
Alcohol, 4; water, 1	Extract of colocynth (N.F. VI).	Powdered.
	Extract of rhubarb.	Powdered.
	Extract of sumbul (N F. VI).	Powdered or soft.
	Extract of valerian (N F. VI).	Powdered.
Alcohol, 3; water, 1	Extract of belladonna.	Soft.
	Extract of hyoscyamus.	Soft.
	Extract of leptandra (N.F. VI).	Powdered.
	Extract of stramonium.	Soft.
Alcohol, 1; water, 7	Extract of taraxacum (N.F. VI).	Powdered or soft.
Alcohol, 75; water, 24; acetic acid, 1; followed by alcohol, 3, water, 1	Extract of nux vomica.	Powdered.
Diluted alcohol, 98, hydrochloric acid, 2, extract defatted	Extract of ergot (N.F. VI).	Soft.
Water	Extract of cascara.	Powdered.
	Extract of gentian (N F. VI).	Powdered or soft.
	Extract of glycyrrhiza, pure.	Soft.
	Extract of opium (N F. VI).	Powdered.
Evaporation of infusion or decoction	Extract of aloe (N.F. VI)	Powdered.
	Extract of beef (N.F. VI).	Soft.
	Extract of malt.	Soft.
Clarification of crude product with alcohol	Extract of ox bile.	Powdered.
Commercial products	Extract of glycyrrhiza.	Powdered or brittle mass.
	Extract of liver.	Powdered.
Admixture of powders	Extract of colocynth, compound (N F. VI).	Powdered.

Of the 12 extracts listed in the U.S.P. XI 6 are powdered, while 6 are soft, the last class including those of pilular consistence; one thin as honey (extract of malt); and one almost brittle (extract of glycyrrhiza). Three of the official powdered extracts (belladonna, hyoscyamus and stramonium) are permitted to be dispensed in pilular consistence as well; the directions for manufacture providing for their preparation in either form. There are 14 N.F. extracts of which 9 are powdered, 3 are powdered or soft, and 2 are soft.

Taking up the several methods of preparing extracts outlined in the table just given, a few words of general explanation of each process may be in place at this time, leaving, of course, minutiæ for consideration under Special Notes.

In the process of *percolation with evaporation*, when the menstruum is hydro-alcoholic, the drug is percolated with the official menstruum and the first portion of the percolate (usually the first 1000 cc. from 1000 Gm. of drug) is put aside as a reserved portion. The remainder of the percolate is evaporated at a low temperature to a very small bulk. With this the reserved portion is mixed, and the mass evaporated to pilular consistence.

The manufacture of extracts by this process is one portion of pharmaceutic manufacturing which cannot be done as well by the retail pharmacist as by the large manufacturer. In order to successfully evaporate the extract at a low temperature—say, 60° C.—it is necessary that a vacuum apparatus be employed, and the cost of such an apparatus precludes its use by the retail pharmacist.

In other cases where alcoholic menstruum is employed, none of the percolate is set aside as reserved portion, but the entire percolate is directly evaporated. This is the case where alcohol, U.S.P., is the menstruum, or where the constituents of the drug are not easily injured by heat. Likewise, if the menstruum is water or a diluted acetic acid, there is no reserved portion, but the entire percolate is evaporated.

When the extract is to be brought to a definite strength, if the finished product is to be a powder, starch is used as the diluent in the present Pharmacopœia while soft extracts are reduced to definite strength by the addition of glucose. Other diluents that may be used with official sanction are malt extracts for pilular extracts and sucrose, lactose, powdered glycyrrhiza, magnesium carbonate, magnesium oxide, calcium phosphate, or the finely powdered marc remaining after the extraction of the drug. Diluents may be colored with chlorophyl or caramel but not to excess.

The process of *evaporation of infusion or decoction* simply consists of extracting the drug with water—either by infusion or decoction—and evaporation of the watery solution either to pilular consistence or to the form of a solid extract by special manipulation. When powdered extracts are made from drugs containing substantial amounts of inactive oily or fatty matter they should be defatted. This may be accomplished by extracting the drug with purified petroleum benzin before percolation or defatting the extract before final adjustment, by stirring and washing with petroleum benzin, draining and then drying the powder below 70° C. Another method is to mix the soft extract with warm acidulated water and allow it to cool, skimming off any oily or fatty matter.

In many respects soft extracts are the least satisfactory of all the official preparations. Thus the phrase, "evaporate to pilular consistence," is rather vague, and the strength of the finished product is apt to be uncertain; not only when first made, but also because, on standing, the strength is apt to change by loss of some of the water the extract contains, the extract becoming hard and dry.

A second factor in the uncertainty of the pilular extracts is the amount of extractive which is contained therein. By the word "extractive" is meant the soluble and inert constituents naturally residing in drugs, grouped, in most textbooks of materia medica, as gums, starches, and sugars. These constituents are practically useless from a therapeutic standpoint, and could they be eliminated, the extract would be much stronger. The question of the quantity of the extractive found in the extracts depends entirely on the menstruum employed, one containing a large amount of water yielding a larger amount of extract than those of a strongly alcoholic nature.

The question of the appropriate menstruum for extracting the full strength of the drug without excess of inert matter has been carefully studied by the Committee on Revision of the Pharmacopœia, and the menstruum directed by that standard is the one yielding the most satisfactory results. This menstruum should, therefore, be strictly followed. Yet there have been unscrupulous manufacturers who deliberately deviate from the pharmacopœial menstruum, adding more water than directed by that standard, in order that large amounts of extract may be obtained. In such cases, of course, an increased yield means a diminution in the active strength of the extract, and it behooves the pharmacist to purchase extracts only from those manufactuers who are known to be reliable.

Among the many constituents which are included in the word "extractive" are the mineral salts, found naturally existing in drugs, such as potassium chloride and sulfate. From many moist extracts on standing the salts crystallize, and such extracts, when rubbed up in making an ointment, are frequently found to be gritty. Whether the grittiness of such extracts is due to crystals or to the accidental mixture of fragments of glass in the container, can be proved by adding a few drops of water and rubbing with an ointment spatula. Should the grittiness dissolve, it shows that it was due to these natural salts; whereas if the grittiness remains after trituration, fragments of glass are indicated.

A third disadvantage in the use of soft extracts is purely pharmaceutic, and that is the inconvenience in handling a semisolid mass. Extracts, especially those of potent drugs, are frequently prescribed in small quantities, say from ¼ to ½ grain. To weigh out the soft extracts it is necessary that the ¼ to ½ grain be weighed on a piece of paper, and by the time the quantity is scraped off the paper and off the spatula, there is frequently very little of the extract transferred to the medicine. It is hardly necessary to say that in weighing such extracts the quantity should be transferred to the paper from the container by means of a perfectly clean spatula, and the spatula cleaned before transferring the weighed portion of the extract into the mortar or other mixture with which it is to be combined. If the surface of paper on which the extract is to be weighed is moistened before "taring," the extract will not stick so closely. Still better is it to use oiled paper or parchment paper.

A fourth inconvenience connected with soft extracts is the uncertainty of the dosage of the extract, due to the uncertainty of the strength of this extract. The variability of the extract strength is of a twofold character: first, different drugs yield vastly differing quantities of extracts. Thus, gum opium yields about half its weight of soft extract; belladonna and hyoscyamus yield about one quarter their weight of extracts, while extract of nux vomica is about six times the strength of the drug.

Hence it is seen that different drugs yield vastly different quantities of extract; not only this, but, worst of all, different batches of the same drug yield different quantities of extract; a very important factor in quality of drugs being the soil on which they have been raised, and particularly the season in which they are collected.

Therefore at their best soft extracts are inconvenient and unreliable, and the revision committee did well in directing that so many of the extracts of the present Pharmacopœia be of definite strength, and that the extracts from potent drugs be assayed.

Strength of Extracts.—As just mentioned, many of the extracts of the present Pharmacopœia are directed to be of definite strength. A list of these standardized extracts is here given:

OFFICIAL ASSAYED SOFT EXTRACTS

Name.	Assayed standard.	Percentage of extract to drug.	Diluent used.
Extract of belladonna.	1.18 to 1.32 per cent total alkaloids.	400	Glucose.
Extract of ergot (N.F. VI).	1 Gm. is equivalent to 2 mg. of ergotoxine ethanesulfonate. Biological assay.	About 400	Starch or glycerin.
Extract of hyoscyamus	0.135 to 0.175 per cent total alkaloids.	350	Glucose.
Extract of stramonium.	1.10 to 1.3 per cent total alkaloids.	About 400	Glucose.

OFFICIAL ASSAYED POWDERED EXTRACTS

Name.	Assayed standard.	Percentage of extract to drug.	Diluent used.
Extract of belladonna.	1.18 to 1.32 per cent total alkaloids.	400	Starch.
Extract of digitalis (N.F. VI).	Biological assay. 0.1 Gm. is equivalent to 3.5 U.S.P. Digitalis units.	350	Starch.
Extract of hydrastis (N.F. VI).	9 to 11 per cent ether-soluble alkaloids.	About 500	Magnesium oxide, 1; starch, 3.
Extract of hyoscyamus.	0.135 to 0.175 total alkaloids.	350	Starch.
Extract of liver.	Clinical assay.		
Extract of opium (N.F. VI).	19.5 to 20.5 per cent anhydrous morphine.	200	Starch.
Extract of nux vomica.	7 to 7.75 per cent strychnine.	700	Starch.
Extract of stramonium.	1.10 to 1.3 per cent total alkaloids.	About 400	Starch.

OFFICIAL STANDARDIZED SOFT EXTRACTS

Name.	Standard.	Percentage of extract to drug.	Diluent used.
Extract of gentian (N.F. VI).	100 Gm. from 200 Gm. drug.	200	Glucose.
Extract of malt.	Will hydrolyze 5 times its weight of starch.		
Extract of sumbul (N.F. VI).	100 Gm. from 300 Gm. drug.	300	Storax.
Extract of taraxacum (N F. VI).	100 Gm. from 300 Gm. drug.	300	Glucose.

OFFICIAL STANDARDIZED POWDERED EXTRACTS

Name.	Standard.	Percentage of extract to drug.	Diluent used.
Extract of aloe (N.F. VI).	100 Gm. from 200 Gm. drug.	200	Starch.
Extract of cascara sagrada.	100 Gm. from 300 Gm. drug.	300	Starch
Extract of colocynth (N.F. VI).	100 Gm. from 400 Gm. drug.	400	Starch.
Extract of colocynth, compound (N.F. VI).	16 per cent extract of colocynth.	....	Resin of ipomea, aloe, cardamom seed
Extract of gelsemium (N.F. VI).	100 Gm. from 400 Gm drug.	400	Magnesium oxide, 1; starch, 3.
Extract of gentian (N.F. VI).	100 Gm. from 200 Gm drug.	200	Starch.
Extract of leptandra (N.F. VI).	100 Gm. from 400 Gm. drug.	400	Starch.
Extract of ox bile.	100 Gm. from 800 Gm. drug.	800	Starch.
Extract of rhubarb.	100 Gm. from 200 Gm. drug.	200	Starch.
Extract of sumbul (N.F. VI).	100 Gm. from 300 Gm. drug.	300	Starch.
Extract of taraxacum (N.F. VI).	100 Gm. from 300 Gm. drug.	300	Starch.
Extract of valerian (N.F. VI)	100 Gm. from 400 Gm. drug.	400	Magnesium oxide 1; starch, 3.

The preservation of extracts should be a matter of more thought than is usually given the subject in the retail pharmacy. Soft extracts should be kept covered tightly to prevent undue evaporation; since this causes them to become hard, dry lumps. An excellent way of keeping extracts is by placing the original containers in which they are obtained from the manufacturer in special extract jars, and thus each extract is protected from the dust.

Powdered extracts—especially those diluted with sugar of milk—should be kept in well-stoppered bottles in a dry place. In contact with moist air they absorb moisture and become sticky masses. All extracts should be protected from strong light.

In such cases desiccation and subsequent pulverization will restore the extract to its original form.

Goris suggests preparation of "unaltered plant extracts" by destroying the oxidizing enzymes found in fresh plants by subjecting these to heated alcohol vapors and then extracting the plants so treated with 80 per cent alcohol and evaporation of alcoholic tincture *in vacuo.*

Commercial extracts—usually prepared by evaporation in a copper vacuum pan—are frequently contaminated with *copper.* This can be detected by sticking a bright steel spatula into the jar of suspected extract and allowing it to remain overnight. If copper is present, a coating of the metal will be found on the spatula in the morning.

Etrat is a new type of extractive preparation that is granular, nonhygroscopic and possessing both the taste and color of the parent drug. These are made by extracting the crude drug with a variety of solvents, the resulting extracts being united, dried under conditions of great caution and finally diluted with the exhausted marc to obtain a granular extract of definite strength. Etrats therefore resemble the abstracts of U.S.P. 1880 (see p. 304).

SPECIAL NOTES ON OFFICIAL EXTRACTS

EXTRACTA—Extracts

The present Pharmacopœia under the heading just given, presents a monograph outlining the manufacture and preservation of solid extracts. Most of the information is covered by what is said on pp. 295 to 297 of this book.

EXTRACTUM BELLADONNÆ—Extract of Belladonna

(**Ext. Bellad.**—Extractum Belladonnæ Foliorum, Extractum Belladonnæ P.I.)

Extract of Belladonna yields, from each 100 Gm., not less than 1.18 Gm. and not more than 1.32 Gm. of the alkaloids of belladonna leaf.

The Pilular Extract

Condensed Recipe.

Belladonna leaves, in No. 40 powder (1000 Gm.) are percolated with the menstruum—alcohol, 3 volumes; water, 1 volume—after sixteen hours' maceration in the packed percolator. After the drug is exhausted the entire percolate is concentrated, first by distillation, then by evaporation below 60° C.; until a pilular extract remains. A portion of this is assayed and the rest is diluted with glucose to the proper alkaloidal strength.

The Powdered Extract

Condensed Recipe.

Belladonna leaves, in No. 40 powder (1000 Gm.) are percolated with the menstruum—alcohol—after sixteen hours' maceration in the packed percolator. The percolate evaporated to pilular consistence below 60° C., is then mixed with dried starch and further heated until it is dry. Assay a portion of the dry extract and dilute the rest with dried starch to the proper alkaloidal strength. The extract must be defatted by one of the two official processes. For details see U.S.P., pp. 154 and 155.

Remarks.—Two methods are given for this extract—one to produce a powdered, the other to produce a soft extract. Both of these are to be diluted to the same alkaloidal strength. A chemical assay process is given.

Dose.—15 milligrams (¼ grain).

EXTRACTUM CANNABIS—Extract of Cannabis

(**Ext. Cannab.**—Extractum Cannabis Indicæ P.I.)

Condensed Recipe.

Take 1000 Gm. cannabis in No. 40 powder, percolate with menstruum—alcohol—after macerating forty-eight hours. Evaporate the percolate to pilular consistence below 70° C.

Remarks.—It will be noted that a biological assay of this preparation was directed in the U.S.P. X but has been discarded in the present Pharmacopœia.

Dose.—0.015 Gm. (1/4 grain).

EXTRACTUM CASCARÆ SAGRADÆ—Extract of Cascara Sagrada (Ext. Casc. Sagr.—Powdered Extract of Cascara Sagrada, Extract of Rhamnus Purshiana)

One Gm. of the extract represents 3 Gm. of cascara sagrada.

Condensed Recipe.

Cascara sagrada, in No. 20 powder (900 Gm.) is treated with boiling water and after three hours' maceration is percolated to exhaustion, adding more boiling water as needed. The percolate is evaporated to dryness on water bath or steam bath and is mixed with enough dried starch to make 300 Gm. Pass through a fine sieve. For details see U.S.P., p. 155.

Remarks.—Unlike the extracts already given, this preparation is diluted to a definite weight and not to a certain strength of active ingredient.

Dose.—300 milligrams (5 grains).

EXTRACTUM FELLIS BOVIS—Extract of Oxbile

(Ext. Fel. Bov.—Powdered Extract of Oxgall)

One Gm. of the extract represents 8 Gm. of oxbile.

Condensed Recipe.

Oxbile (800 Gm.) is evaporated to 200 cc. and to this 500 cc. of alcohol are added slowly with constant stirring. After twenty-four hours the liquid portion is decanted, and the residue is mixed with 250 cc. of alcohol, filtered and the filter washed with 250 cc. of alcohol. The combined alcoholic liquid is then evaporated at 80° C. to dryness. The dried extract is then powdered and mixed with enough dried starch to make 100 Gm. For details see U.S.P., p. 156.

Remarks.—This extract is merely a modification of *purified oxgall* of the older Pharmacopœias. It consists of oxbile dissolved in alcohol to remove the mucin and other slimy bodies and after decantation and filtration, the alcohol is evaporated off, the residue dried and brought to a definite strength by dilution with starch. It is an improved form of the old-fashioned inspissated oxgall.

Dose.—0.4 Gm. (6 grains).

EXTRACTUM GLYCYRRHIZÆ—Extract of Glycyrrhiza

(Ext. Glycyrrh.—Extract of Licorice Root, Licorice)

A commercial Extract of Glycyrrhiza prepared from the rhizome and roots of species of *Glycyrrhiza* (Fam. *Leguminosæ*) and having a sweetish taste which is not more than very slightly acrid.

Description.

This extract of licorice occurs as a brown powder or in cylindrical rolls or masses. At least 60 per cent must dissolve in cold water. It must be free from foreign starches. Ash, not more than 8 per cent.

Manufacture.—Prepared on a large scale in Italy by evaporating a strained aqueous infusion in vacuum pans, and rolling the extract while still soft into sticks. It must be free from foreign starches.

Remarks.—This extract is the commercial product known as "stick licorice." Samples found in the market are frequently adulterated with starch, dextrin and other insoluble matter; hence the pharmacopœial requirement that at least 60 per cent be soluble in cold water.

EXTRACTUM GLYCYRRHIZÆ PURUM—Pure Extract of Glycyrrhiza

(Ext. Glycyrrh. Pur.—Pure Extract of Licorice Root)

Condensed Recipe.

Moisten 1000 Gm. glycyrrhiza, in No. 20 powder, with boiling water, then pack and percolate with boiling water to exhaustion. Concentrate the percolate to one half its volume by boiling, filter, and finally evaporate the filtrate on a water bath to pilular consistence. For details see U.S.P., p. 157.

Remarks.—This extract is prepared by percolating the drug with boiling water. A temperature of 100° C. is desirable in order to eliminate material of an albuminous nature. Note that the commercial *purified extract of licorice* is usually in powdered form, hence not identical with the official product.

In former Pharmacopœias, ammonia water was usually employed in the menstruum for licorice preparations, owing to the belief that the sweet principle, glycyrrhizin (p. 716) is more soluble in alkaline fluids.

EXTRACTUM HEPATIS—Extract of Liver

This extract is discussed under Animal Drugs in Chapter LI.

EXTRACTUM HYOSCYAMI—Extract of Hyoscyamus

(Ext. Hyosc.—Extract of Henbane, Extractum Hyoscyami P.I.)

Extract of Hyoscyamus yields, from each 100 Gm., not less than 0.135 Gm. and not more than 0.175 Gm. of the alkaloids of hyoscyamus.

Condensed Recipe.

Hyoscyamus, in No. 40 powder, is made into a pilular extract by the same procedure followed in making soft extract of belladonna. Powdered extract made like powdered extract of belladonna is also recognized in U.S.P. XI. For details see U.S.P., pp. 157, 158.

Dose.—0.05 Gm. (5/6 grain).

EXTRACTUM MALTI—Extract of Malt

(Ext. Malt.)

Extract of Malt is a product obtained by extracting malt, the partially and artificially germinated grain of one or more varieties of *Hordeum vulgare* Linné (Fam. *Gramineæ*). The malt is infused with water at 60° C., the expressed liquid concentrated at a temperature not exceeding 60° C., and the extract mixed with 10 per cent, by weight, of glycerin. It contains dextrin, maltose, a small amount of glucose, and amylolytic enzymes.

Extract of malt is capable of converting not less than five times its weight of starch into water-soluble sugars.

Description.

A sweet water-soluble light-brown viscous extract with agreeable characteristic odor. Specific gravity, 1.35 to 1.43 at 25° C.

Remarks.—This is the popular pharmaceutical soft extract of malt and must not be confused with the more or less fermented liquid extract of malt, prepared by brewers. Note that U.S.P. XI provides an assay based upon the ability of the diastase (p. 953) in the extract to convert starch into water-soluble sugars.

Dose.—15 Gm. (4 drachms).

EXTRACTUM NUCIS VOMICÆ—Extract of Nux Vomica

(**Ext. Nuc. Vom.**—Powdered Extract of Nux Vomica, Extractum Strychni P.I.)

Extract of Nux Vomica yields, from each 100 Gm., not less than 7 Gm. and not more than 7.75 Gm. of strychnine.

Condensed Recipe.

Moisten 1000 Gm. Nux Vomica, in No. 40 powder, with the menstruum—alcohol, 75 volumes; water, 24 volumes; acetic acid, 1 volume. Macerate twenty-four hours after packing and then percolate to exhaustion with a menstruum of alcohol, 3 volumes; water, 1 volume. Evaporate the percolate below 100° C. to 200 cc. Add 150 cc. of water and about 200 cc. of purified petroleum benzin. Agitate frequently during half an hour. Separate and reject the benzin and wash the aqueous mixture with another portion of 150 cc. of purified petroleum benzin. Separate and reject the benzin. The aqueous fat-free liquid is then evaporated to dryness below 60° C. A portion of the dry extract is then assayed and the rest is diluted with starch to the proper alkaloidal strength. For details see U.S.P., p. 160.

Remarks.—This extract is freed from fat with petroleum benzin.

Dose.—0.015 Gm. (¼ grain).

EXTRACTUM RHEI—Extract of Rhubarb

(**Ext. Rhei**—Powdered Extract of Rhubarb)

Each Gm. of the extract represents 2 Gm. of rhubarb.

Condensed Recipe.

Moisten 1000 Gm. rhubarb in No. 40 powder with the menstruum—alcohol, 4 volumes; water, 1 volume. After maceration for forty-eight hours percolate with the menstruum to exhaustion. Evaporate the percolate to dryness at 70° C. and then add enough starch to make the product weigh 500 Gm. Pass through a fine sieve. For details see U.S.P., p. 160.

Dose.—0.5 Gm. (8 grains).

EXTRACTUM STRAMONII—Extract of Stramonium

(Ext. Stramon.)

Extract of Stramonium yields, from each 100 Gm., not less than 1.1 Gm. and not more than 1.3 Gm. of the alkaloids of stramonium.

Manufacture.—Both soft and powdered extracts of stramonium are directed and the recipes given in the Pharmacopœia are identical with those for extract of belladonna. See U.S.P., p. 160.

Dose.—0.02 Gm. (⅓ grain).

DOSES OF OFFICIAL EXTRACTS

10 mg. (⅙ grain)	Extract of gelsemium (N.F. VI).
15 mg. (¼ grain)	Extracts of belladonna, cannabis, and nux vomica.
20 mg. (⅓ grain)	Extract of stramonium.
30 mg. (½ grain)	Extracts of colocynth (N.F. VI), digitalis (N.F. VI), and opium (N.F. VI).
50 mg. (⅚ grain)	Extract of hyoscyamus.
125 mg. (2 grains)	Extract of aloe (N.F. VI).
250 mg. (4 grains)	Extracts of colocynth compound (N.F. VI), leptandra (N.F. VI), and valerian (N.F. VI).
300 mg. (5 grains)	Extract of cascara sagrada.
400 mg. (6 grains)	Extract of ox bile.
500 mg. (8 grains)	Extracts of ergot (N.F. VI), gentian (N.F. VI), hydrastis (N.F. VI), rhubarb, and sumbul (N.F. VI).
1 Gm. (15 grains)	Extract of taraxacum (N.F. VI).
15 Gm. (4 drachms)	Extract of malt.
To be stated upon label of container	Extract of liver.
No dose given	Extracts of glycyrrhiza, glycyrrhiza pure, and beef.

Extractum Aconiti (U.S.P. IX) or *Powdered Extract of Aconite*, is made by percolation of the drug with alcohol containing a small amount of tartaric acid. The extract obtained on evaporation of the percolate is then defatted by treatment with purified petroleum benzin after which it is diluted with starch, dried on glass plates, assayed and then brought to the proper strength by adding more starch. *Dose.*—0.010 Gm. (⅙ grain).

Extractum Cimicifugæ (U.S.P. IX), or *Powdered Extract of Cimicifuga*, is made by percolating the drug with alcohol, recovering the alcohol by distillation, evaporating the residue to dryness and then mixing it with enough starch to make a powdered extract, 1 Gm. of which represents 4 Gm. drug. *Dose.*—0.25 Gm. (4 grains).

Extractum Colchici (U.S.P. X) or *Extract of Colchicum* a powdered extract containing 1.25 to 1.55 per cent colchicine is made from colchicum corm, by percolation with alcohol—after maceration for forty-eight hours in the packed percolator. The entire percolate is distilled and the residue is shaken out with three portions of purified petroleum benzin. The residue thus treated is concentrated on a water bath to a thick extract, is mixed with dried starch and is then dried on glass plates in an air bath at 70° C. A portion of the dried powdered extract is assayed and the rest is diluted with dried starch to the proper alkaloidal strength. *Dose.*—0.6 Gm. (1 grain).

Extractum Colocynthidis (U.S.P. X; N.F. VI) or *Extract of Colocynth* is a powdered extract in which 1 Gm. represents 4 Gm. of colocynth. It is made from colocynth in No. 20 powder, by percolation with a menstruum of alcohol, 4 volumes; water, 1 volume, evaporating the percolate to dryness, diluting with sufficient starch to make the extract weigh one fourth the amount of drug used.

Extractum Colocynthidis Compositum (U S.P X; N.F. VI) or *Compound Extract of Colocynth* is a powdered extract made by mixing and sifting extract of colocynth, 160 Gm.; aloe, 650 Gm.; cardamom seed, 50 Gm.; resin of ipomœa, 140 Gm. The latter three should all be in No. 60 powder. This, the only official compound extract, is prepared by blending extract of colocynth with aloe, cardamom seed, and resin of ipomœa. The U.S.P. X formula included powdered soap which was added partly to increase the purgative properties, but chiefly in order that the finished product could be worked into a pill-mass by the addition of water. *Dose.*—0.25 Gm. (4 grains).

Extractum Ergotæ (U.S.P. IX; N.F. VI) or *Extract of Ergot*, is prepared by first defatting the ergot by percolation with purified petroleum benzin, after which it is percolated with an acidulated hydro-alcoholic menstruum and the percolate is finally concentrated to a soft extract. *Ergotin* is an aqueous extract of ergot. A recipe for such a preparation was given in the National Formulary V. *Dose.*—0.5 Gm. (8 grains).

Extractum Gelsemii (U.S.P. IX; N.F. VI), or *Powdered Extract of Gelsemium*, is made by percolating the drug with alcohol, evaporating the residue at 70° C. to a soft extract and finally mixing it with enough magnesium oxide and starch and evaporating to make a powdered extract, 1 Gm. of which represents 4 Gm. drug. *Dose.*—0.01 Gm. (⅙ grain).

Extractum Gentianæ (U.S.P. IX; N.F. VI), or *Extract of Gentian*, is made by the evaporation of the cold aqueous percolate from gentian, this liquid being strained after concentrating, and then evaporated to pilular consistence, using glucose to make each gram of extract equal 2 Gm. of drug. The use of the extract as a routine pill excipient, so popular in the South, is not to be recommended from the medical point of view (p. 331). *Dose.*—0.5 Gm. (8 grains).

Extractum Hydrastis (U.S P. IX; N.F. VI), or *Extract of Golden Seal*, is made by percolating the drug with the menstruum—alcohol—evaporating at 70° C., mixing the soft extract with magnesium oxide and starch, assaying and finally diluting with magnesium oxide and starch to the proper alkaloidal strength; 9 to 11 per cent of ether-soluble alkaloids of hydrastis. *Dose.*—0.5 Gm. (8 grains).

Extractum Opii (U.S.P. IX; N.F. VI), or *Powdered Extract of Opium*, is made by percolating or macerating opium with hot water, then evaporating to dryness at 100° C. The dry extract is then assayed and enough starch is added to bring the finished product to the proper alkaloidal strength; 19.5 to 20.5 per cent of anhydrous morphine. *Dose.*—0.03 Gm. (½ grain).

Extractum Physostigmatis (U.S.P. IX), or *Powdered Extract of Physostigma*, is made by extraction of the drug, first with tartaric acid, alcohol and water and then with alcohol and water. The manipulation resembles the manufacture of extract of aconite. *Dose.*—0.008 Gm. (⅛ grain).

Extractum Sumbul (U.S.P. IX; N.F. VI), or *Extract of Sumbul*, is made by percolating the drug with a mixture of 4 volumes of alcohol and 1 volume of water, evaporating the percolate at 70° C. and mixing with storax to bring to the equivalent of 1 Gm. of extract for each 3 Gm. of drug. The powdered extract is made by mixing with magnesium oxide and starch and drying to a pilular consistence. *Dose.*—0.5 Gm. (8 grains).

Extractum Taraxaci (U.S.P. IX; N.F. VI), or *Extract of Taraxacum,* is made by extraction of the drug with 1 volume of alcohol and 7 volumes of water, the procedure resembling the manufacture of extract of sumbul. The powdered extract is likewise made like extract of sumbul. *Dose.*—1 Gm. (15 grains).

Extractum Viburni Prunifolii (U.S.P. IX), or *Powdered Extract of Viburnum Prunifolium,* is made by percolating the drug with diluted alcohol, recovering the alcohol by distillation, evaporating the residue to dryness and mixing with enough magnesium oxide and starch, to make a powdered extract, 1 Gm. of which represents 5 Gm. drug. *Dose.*—500 milligrams (8 grains).

EXTRACTS OF THE NATIONAL FORMULARY

Name.	Consistence.	Menstruum.	Drug extracted by.	Diluent.	Strength.	Remarks.
Aloe . . .	Powdered.	Boiling water.	Maceration.	Starch.	200 per cent of drug.	
Beef.......	Soft.	Water.	Cooking.	None.	No mention.	
Colocynth	Powdered.	Alcohol, 4; water, 1.	Percolation.	Starch.	400 per cent of drug	
Colocynth, compound	Powdered.	None.		Resin of ipomœa, aloe; cardamom seed.	16 per cent of extract of colocynth.	
Digitalis	Powdered.	Alcohol.	Percolation	Starch.	350 per cent of drug	
Ergot . .	Soft	Diluted alcohol, 98, hydrochloric acid 2.	Percolation.	Starch or glycerin.	About 400 per cent of drug	
Gelsemium.	Powdered.	Alcohol.	Percolation.	Magnesium oxide, 1; starch, 3	400 per cent of drug.	
Gentian ...	....	....	....	......	....	See p. 303.
Hydrastis .	....	....	....	....	....	See p. 303.
Leptandra	Powdered.	Alcohol, 3, water, 1.	Percolation.	Starch.	400 per cent drug.	*Dose* —250 milligrams (4 grains)
Opium. . .	....	..	.....	.....	.....	See p. 303.
Sumbul	.		.	..		See p. 303.
Taraxacum	....	...	....	.....	.	See above.
Valerian	Powdered	Alcohol, 4; water, 1	Percolation	Starch, 3; magnesium oxide, 1.	400 per cent of drug.	

ABSTRACTS

Abstracts, a class of preparations introduced into the Pharmacopœia of 1880, intended to supplant extracts, were powders containing the active principles of drugs in condensed form, and of definite strength, prepared by percolating the drug with the appropriate menstruum, reserving a certain portion (say, 90 per cent of the weight of the drug), evaporating the weak percolate of the drug to a thin extract, blending with the reserve portion and also with sugar of milk; evaporating the mixture at a low temperature until dry. The mass was then weighed, and enough sugar of milk added to make the finished product exactly half the weight of the drug from which it was derived. Such an abstract, therefore, represents twice the strength of the drug.

Abstracts possess over soft extracts the great advantage of being in powdered form and of definite and uniform strength, but, unfortunately, they won little favor from physicians and were dropped in the revision of 1890. Their advocacy was not in vain, however, since in the present Pharmacopœia, as already mentioned on page 297, most of the official extracts are in powdered form and twenty-three of the twenty-six are standardized.

RESINS

While in the chemical sense resins are solid plant substances or exudations usually acid in character, insoluble in water, but soluble in water plus alkali, the definition of the pharmaceutic class—resins—are *those plant products, soluble in alcohol and insoluble in water, obtained either as the residue from the distillation of an oleoresin, or by pouring a concentrated alcoholic extract of a drug into water or acidulated water.* All three official resins are made by the latter process; but, as example of resins obtained by distillation of an oleoresin, may be cited resin of copaiba (U.S.P. 1890) and official rosin. The latter, however, can best be considered as a crude drug, and is, therefore, discussed in Part IV.

SPECIAL NOTES ON OFFICIAL RESINS

RESINA PODOPHYLLI—Resin of Podophyllum

(Res. Podoph.—Podophyllin)

Storage.—Preserve in well-closed containers and protected from light.

Condensed Recipe.

Percolate 1000 Gm. podophyllum, in No. 60 powder with alcohol to exhaustion; concentrate the percolate by evaporation to a thin syrup, which is then poured into a mixture of 10 cc. of hydrochloric acid with 1000 cc. of water, which has been chilled to 10° C. Let the precipitated resin subside, decant the supernatant fluid; wash the precipitate by decantation, with two portions of cold water; and then collect and dry and powder it. For details see U.S.P., p. 319.

Condensed Description.

Amorphous powder; light-brown to greenish-yellow; peculiar odor; bitter taste; soluble in alcohol; 75 per cent is soluble in ether; 65 per cent is soluble in chloroform; hot water extracts some bitter principle which turns brown with ferric chloride; soluble in fixed alkaline hydroxides, with a yellow color; ash, not more than 1.5 per cent.

Impurity.—The resin from *Podophyllum Emodi.* See U.S.P., p. 319.

Remarks.—This is the only resin now included in the Pharmacopœia. The question of temperature and composition of the precipitation liquid is of great importance in making this and other resinoids. Some manufacturers precipitate podophyllin by pouring into alum solution, securing a larger yield and a less active product. Unless the precipitation is properly conducted there is danger of obtaining a markedly toxic product.

This resin is the most important of the so-called "*resinoids*," a class of preparations introduced by eclectic practitioners, through whose efforts a large number of valuable American drugs—such as podophyllum and hydrastis—were brought to the attention of physicians.

In attempting to secure concentrated forms of these eclectic drugs Dr. King hit upon the idea of extracting the drug with strong alcohol and pouring this alcoholic tincture into water. In this way he obtained resin of podophyllum, and so named it. Later manufacturers, supposing it a definite body, called it "podophyllin."

Like many other excellent ideas, the search for such concentrates was carried to excess, and thus were put upon the market a number of *resinoids*, each purporting to be the active principle of the plant from which derived, and given the name implying such active constituent. Among such resinoids of little or no value may be cited *aletrin* (from *Aletris farinosa*); *geranin* (from *Geranium maculatum*); *macrotin* (from *Cimicifuga racemosa*, the other botanical name of which is *Macrotrys actæoides*); and *sanguinarin* (from *Sanguinaria canadensis*). How these commercial names lead to confusion can best be shown by the statement that the resinoid, sanguinarin, has nothing in common with sanguinarine, the alkaloid of sanguinaria.

Resin of podophyllum is a constituent of a number of pills included in the National Formulary. (See p. 341.) It is not used, however, in any preparation of the present Pharmacopœia.

Dose.—0.01 Gm. (1/6 grain).

Resina Ipomœæ (U.S.P. X; N.F. VI) or *Resin of Ipomœa,* also known as *resin of Mexican scammony* is made by extracting ipomœa in a No. 40 powder with the menstruum—alcohol, 9 volumes, water, 1 volume—concentrating the percolate to a thin syrup and pouring this slowly into twice its volume of hot water. The precipitate is allowed to settle and is washed with hot water by decantation and finally the resin is dried. It occurs in brown translucent masses; characteristic odor; soluble in alcohol and chloroform; 80 to 90 per cent should dissolve in ether; ash, not more than 0.5 per cent. Rosin, guaiac and other resins; aloin; water-soluble matter are possible impurities. Resin ipomœa replaces resin of scammony formerly official but difficult to obtain during the World War (p. 721). *Dose.*—0.2 Gm. (3 grains).

Resina Jalapæ (U.S.P. X; N.F. VI) or *Resin of Jalap* is made by extracting the resin from jalap in No. 60 powder with a mixture of alcohol, 9 volumes, water, 1 volume, concentrating the percolate to about one fourth the weight of drug taken and pouring slowly into about 12 times as much water. The precipitate is collected, washed with hot water and then thoroughly dried. This resin occurs in yellow to brown masses or fragments; peculiar odor, acrid taste; soluble in alcohol; insoluble in carbon disulfide; not more than 30 per cent should dissolve in chloroform. Rosin, guaiac and other resins; aloin; water-soluble matter are possible impurities. *Dose.*—0.125 Gm. (2 grains).

Resina Scammoni (U.S.P. IX) is made from scammony root by a method almost identical with that described in resin of ipomœa, which replaces this. As explained under ipomœa and scammony root (p. 721) the latter drug has become so scarce since the World War, that the more easily obtainable drug, ipomœa has been substituted for it. *Dose.*—200 mg. (3 grains).

Resina Copaibæ (U.S.P. 1890) was included in a number of the editions of the United States Pharmacopœia but was dropped in the eighth revision. It is made by distilling the oleoresin, copaiba, when the volatile oil passes over, leaving the resin in the retort.

BIBLIOGRAPHY

Inspissated Juices.—Anon., Ph. Jl. [4], 12, 1901, 158 and 259.

Extracts.—(Manufacture) Herrera, Ph. Jl. [3], 8, 1877, 283. Simon, Ph. Jl., 107, 1921, 519. (Copper contamination) Shuler, Pharm. Era, 1, 1887, 361. (Powdered) Hallberg, A.Ph.A., 29, 1881, 424. ("Unaltered") Goris, Spatula, 16, 1890, 21; Beguin, Ph. Acta Helv., 4, 1929, 202 and 213. (Colocynth compound) "X-rayser II, Dr. Circ., 58, 1914, 281. (Gentian) Guibourt, Jl. de ph., 9, 1823, 285. (Licorice) Parry, A.Ph.A., 58, 1910, 80; Houseman, A.J.P., 84, 1912, 531; 88, 1916, 97 and 93, 1921, 481; Griebel and Weiss, Apoth. Zt., 45, 1930, 1566. (Malt) Hamburg, Ph. Jl. [4], 83, 1909, 133. Sage, Ch. and Dr., 113, 1930, 53.

Etrats.—Eschenbrenner, Ph. Zt., 75, 1930, 1215; Grimme, Ph. Zent., 71, 1930, 657 and 72, 1931, 193; Kroeber, Apoth. Zt., 46, 1931, 360.

Abstracts.—Coblentz, A.Ph.A., 33, 1885, 424.

Resins.—(Eclectic resinoids) Little, A.Ph.A., 25, 1877, 97; Lloyd, A.Ph.A., 35, 1887, 65; Dr. Circ., 47, 1903, 4; Ough, Ch. and Dr., 51, 1897, 524; 52, 1898, 86 and 548; 53, 1898, 183; 55, 1899, 299 and 561; 56, 1900, 158 and 735; Parker, Ph Jl. [3], 12, 1881, 41 and 62. (Podophyllum) Lloyd, A.J.P., 62, 1890, 242; Scoville, A.Ph.A., 57, 1909, 897.

CHAPTER XVIII

POWDERS AND TRITURATIONS

POWDERS

A DEFINITION for powders is somewhat difficult unless we are satisfied with the rather vague statement, *combinations of solid drugs in finely divided form.*

It is even questionable whether powders should be grouped under "internal preparations," for while all official powders are used internally, there are many prescriptions for powders intended for dusting purposes. Powders are usually made by trituration with pestle and mortar, though dusting powders should be made by mixing the ingredients, already reduced to a fine powder, with a spatula, since rubbing in a mortar is apt to cause caking.

In writing prescriptions for compound powders the physician usually directs the trituration of a sufficient quantity of the ingredients to make several powders. This is particularly useful from the point of the physician in enabling him to prescribe a certain weighable quantity of a potent drug, say, 1 grain of arsenic, and directing that to be rubbed up with the other constituents, and then to be dispensed in a sufficient number of parts, so that each part will contain a safe dose. Thus, if a grain of arsenic is directed in 30 powders, each powder will contain the usual dose of that chemical ($\frac{1}{30}$ grain). In preparing such powders it is necessary for the pharmacist to exert great caution in having the potent ingredient sufficiently triturated with the diluent to insure uniform and thorough subdivision.

Proper trituration is a matter of experience and skill. Some powders rubbed together in a mortar by a pestle become electrified. This can be prevented by the addition of a few drops of alcohol. Some liquefy (see "cryoscopic substances," p. 832). The liquefaction can sometimes be prevented by the addition of 1 per cent of lycopodium. The prescribing physician should be notified as to the reason of such a modification of his orders.

The dividing of the mass into the requisite number of powders is accomplished in several ways. In one the papers, which are to hold the several portions of the divided powder, are spread on a clean table; the mixture transferred to the papers in portions by means of the spatula, and when all the substance has thus been transferred, an attempt is made to equalize the quantity of powder on each paper by means of the eye. With practice one becomes fairly expert at striking the requisite quantity, although the process, at its best, is inaccurate, as can be proved by any pharmacist by taking at random 3 or 4 powders from the batch that is thus divided and weighing each. A variation of 25 to 30 per cent is not unusual.

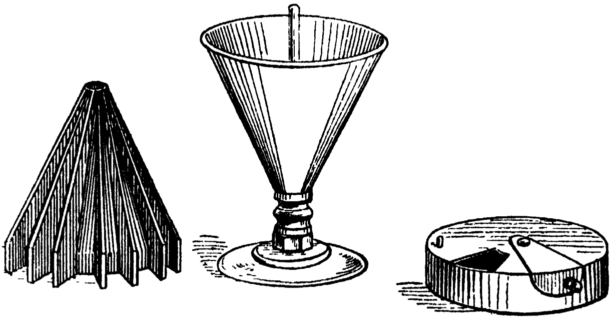


Fig. 193.—Michael's powder divider.

In order to render the subdivision more accurate, several appliances for the dividing of powders have been devised. Of these the most convenient is the Michael powder divider (Fig. 193). This consists of a tapering cup into which the mixed powder is poured and packed fairly uniformly by gentle tapping. Into this is then inserted a special separator consisting of metal segments, which exactly divide the cup into the number of powders desired, thus equally dividing the powder into the desired portions. This being done, the apparatus is covered with a tightly fitting cap, provided with one orifice, through which the contents of compartments of the divider can be poured off one at a time. By turning the cap so that the orifice changes from segment to segment, and inverting after each case, the contents of each segment can be emptied. At its best, however, such a powder divider is not exceedingly convenient, nor is it so correct as one would wish.

The third, and by all odds the best, method of dividing powders is by calculating the weight that each powder should be, and weighing out that quantity, and transferring it forthwith to one of the unfolded papers. In this way correct results are obtained, and when once practiced, the process is found to demand but little more time than that consumed in dividing by eye. In weighing powders it is found, however, by reason of the extreme accuracy of the process, that the last powder is apt to be short in weight, due to the natural loss because of some of the powder adhering to the pestle and mortar. In the writer's practice he always weighed out a sufficient amount of each ingredient called for in the prescription to make one more powder than the number directed, and the slight excess, after weighing out the requisite number of papers, was then thrown away. The powders so divided are then folded in separate pieces of paper; the art of "powder-folding" being one acquired with a little practice. The process consists in laying upon a clean table, the requisite number of papers, each provided with a fold at the top, the size of which has been determined in advance. The subsequent processes will best be shown in the appended illustrations (Fig. 194), the second stage being to bring up the lower edge of the paper to the crease already made, as shown in *b*. The flap of the crease is then bent over on to the edge, the paper then taken and creased and folded down to the lower edge of the paper, and then all that remains is that the two edges be folded inward, as shown in *c*. The folding of these ends, so that the length of each folded paper be the same, is sometimes performed on a special powder-folder, shown in Fig. 195, although many careful pharmacists fold the paper as directed upon the box into which the finished powders are to be placed.

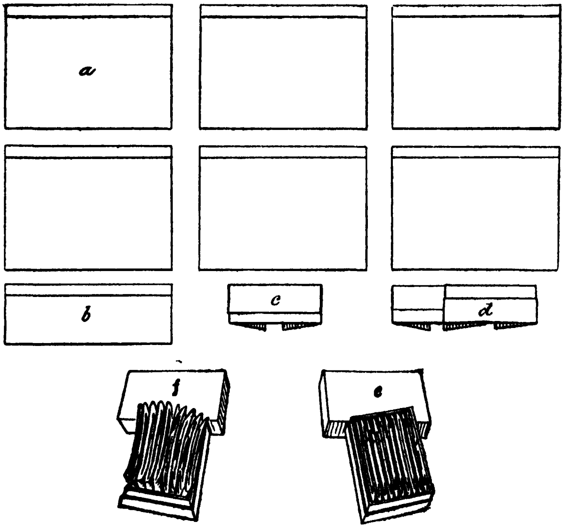


Fig. 194.—Folding powders (see text).

There are now on the market powder papers folded by machinery and intended to be used by opening, putting in the powder, and folding again, but the writer fails to see wherein these give better results than a plain paper folded by hand, as directed below.

In discussing the question of the various forms of powder boxes, it is necessary here to say that modern pharmacists use the so-called "New York powder box," shown in Fig. 196, slide powder boxes failing to give as good results. Into this New York powder box the powder should be placed upright, as is shown in Fig. 194*e*, and in folding the powder each should be exactly the same size, and should project from the box to the same height—usually made about 1/16 inch. The finer grade of the powder box is arranged with a sufficient difference between the height of the shoulder and of the inside of the cover to permit the papers to protrude that distance, the object of having the papers protrude being to facilitate the removing of the papers from the box. A useful modification of the New York powder box is the hinged type. This prevents the possibility of the covers of boxes (bearing prescription number and directions for the patient) from being mixed.

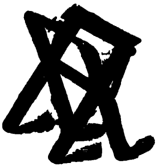


Fig. 195.—Powder folder.

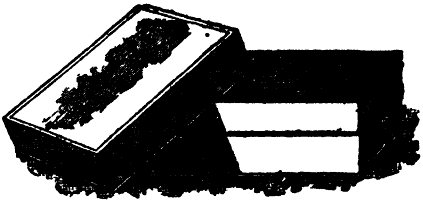


Fig. 196*a*.—New York powder box.

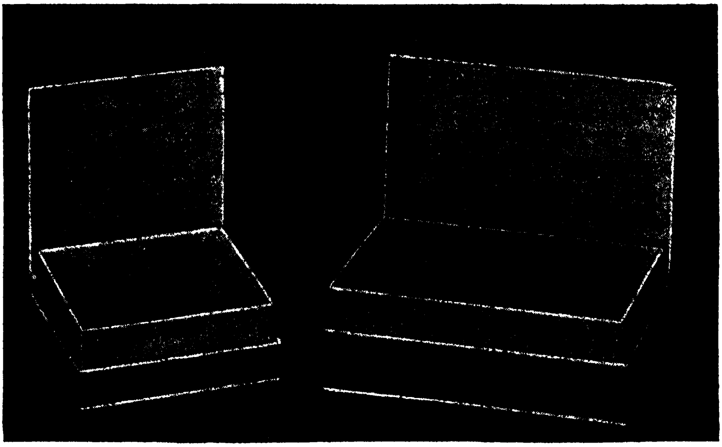


Fig. 196*b*.—Hinged type powder box.

In preparing and successfully folding the paper it is necessary that the paper conform exactly to the dimensions of the box, and in order to aid the pharmacist in this work, the so-called "shoulder boxes" are made the same length and height, the difference in the size for the different numbers of papers being merely in the width. In purchasing boxes of that kind the pharmacist should procure paper of such size as will make a perfectly neat package; that is, a paper the length of which is a trifle less than double the interior length of the box, while the width of the paper should be a little over twice the height of the box. Having obtained paper of the right dimensions, all that remains to be done is to learn the size which the first flap (Fig. 194) should be made. This is so regulated that the powder, when folded, with the end where the original flap was made coinciding with the finished folded paper, will make a finished powder of the height suggested above, namely, one which will protrude 1/16 inch from the paper box.

Having folded a paper to conform with the size of the box, it is customary to make the finished powder smooth by rubbing each end down with a spatula. The powders are then gathered up from the counter and piled together with the flaps alternating up and down (Fig. 194). These precautions are required because it will be seen that the finished powder is thicker where the flap rests than in any other portion of the paper. If the bunch of powders, say 12 to 24, were placed in a box, all in the same position, this slight increase in thickness, multiplied by the number 12 or 24, would make a decided discrepancy in the width of the top and bottom of a bunch of powders; and if such were placed in the box in which they fit snugly, a decided pressure would be exerted at the upper edge, a pressure, in fact, sufficient to cause the springing out of the entire lot of powders when the first paper was removed (Fig. 194). By alternating the position of the flap up and down the pressure is equalized and no such inconvenience results.

Some pharmacists follow the admirable custom of having their name and address printed on their powder papers in such a position that the printed matter will appear in the center of the folded paper. Such a practice cannot be too strongly recommended, because it affords a highly legitimate method of publicity.

After the powders are neatly folded and placed in the box, the latter is wrapped in an appropriate paper and tied. This leads us to the very important question of the dispensing of packages in elegant form, an art which appears to the writer to be falling into disuse. The first essential in making a successful package is that the paper be of exactly proper proportions, and the writer attributes to the introduction of the roll paper, so largely used in drug stores at present, and supposed to be unrolled and torn off as required, the lack of care shown in the modern package.

In former days the paper was bought in full sheets and was carefully cut to the size required for the package. Thus, for powder boxes the paper was cut in strips 4 inches wide, and of a length ranging from 6 to 8 inches. For pill boxes smaller strips, say 2½ inches wide, were employed. The paper for 1-ounce bottles was 6 by 6 inches, for 2- and 3-ounce bottles was 7 by 8½ inches; for 4- and 6-ounce bottles was 8½ by 11 inches; for 8-ounce bottles was 11 by 11 inches; while for pint bottles it was 12 by 12 inches. Of the paper so cut, the one for 6-ounce bottles usually sufficed for the careful wrapping of 1 to 2 ounces of an herb, and from 4 to 8 ounces of a chemical; while the larger sized papers would be used for proportionately larger quantities. The criticism that might be raised in regard to taking pains in making packages is the time which is required. As far as the wrapping of a powder or pill box or of a bottle, no more time is required for wrapping it carefully than is required to do the same work carelessly, and as for the wrapping of solid substances, it is recommended that the pharmacist follow the custom of old-time druggists of keeping on hand a sufficient stock of packages already wrapped, which can be handed out when demanded. In the author's experience, he kept on hand packages of almost everything for which there was at least one demand a week. Of those substances for which there was a very slight demand, only one package was prepared and kept in the container, and when this was sold, another package was made at the first leisure moment. In this way the pharmacist, especially when by himself in a store, can facilitate dispensing to an enormous extent, because much time is consumed in wrapping packages. Details of making a neat package can be best given accompanied by the following illustrations:

Wrapping a pill box: Take the strip of paper, place the pill box thereon, and bring up the two ends, and fold over into a crease, as is shown in Fig. 197*a*. The paper should be made of such a size that a second crease about the size of the first one will bring the paper perfectly firmly around the edge of the pill box, as shown in *b*. The paper should then be of such width that when the edges are folded down in the flap, there will be no bulging pieces of paper to be cut off. In the writer's experience, he preferred folding the open edges down to the folded flaps, as shown in *c*, because when so done the tying can be done by simply passing the string two or three times around the edge of the box, as is shown in *d*. Some pharmacists prefer to bring the edges down, as is shown in *e*, when the string must be placed, not around the edges, but over the top of the box, as is shown in *f*. In place of twine, elastic bands are now used, and have much to commend themselves.

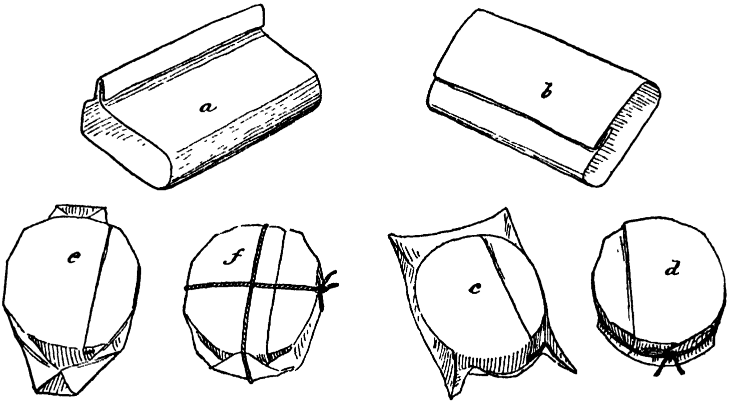


Fig. 197.—Wrapping pill box (see text).

In wrapping a powder box the procedure is similar to that of a pill box, as shown in the various stages in Fig. 198*a* and *b*. The flaps are folded either as shown in *c* or *d*, and for the same reason as explained in the case of the pill boxes.

In wrapping bottles the mode of procedure is, first, to fold the crease, as shown in Fig. 199*a* and, as in the case of the powder and pill boxes, the paper should be of such a size that the second fold will bring the paper snugly around the bottle, as shown in *b*. The open edge at the base of the bottle is then folded in neat flaps, while the paper around the neck should be creased, as shown in *c*.

This done, the bottle is wrapped with string down and back, and finally wound tightly around the neck, as is shown in *d*.

In folding packages the paper is first folded with the crease, as shown in Fig. 200*a*. This crease is then bent, very great care being required to make it exactly equal the whole length of the package, as shown in *b*. One of the open ends is then temporarily folded, as shown in *c*, while the other end is carefully folded away from the flap, as shown in *d*. This being done, it is then turned downward, the temporary folding of the other end reopened, and refolded exactly as the other end, the finished package is then wrapped with a string, both across its length and width as shown in *e*, although for this purpose a rubber band is frequently substituted.

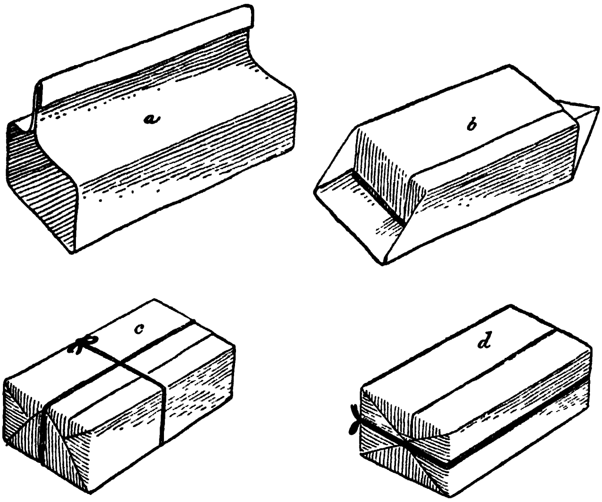


Fig. 198—Wrapping powder box (see text).

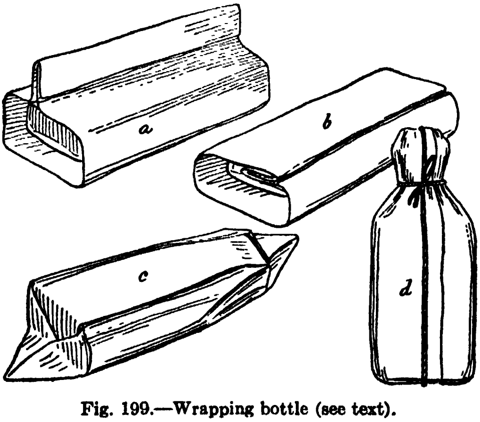


Fig. 199.—Wrapping bottle (see text).

The folding of solids in packages, as just mentioned, is becoming obsolete, due to the introduction of boxes for holding solid substances, at prices justifying their free distribution by the druggist.

Such boxes should be wrapped with paper in a manner similar to the smaller powder boxes, and the use of such boxes is growing very popular because of the convenience of keeping drugs in such containers. It might be here stated that all packages of drugs and chemicals wrapped in the style above given should be neatly labeled.

As to the choice of wrapping-paper, the writer uses plain white paper in preference to the gaudily colored papers so much in vogue in modern pharmacies. He is not alone in this preference, for not long since a woman of refinement and culture spoke of the shocking lack of taste displayed by the average druggist in dispensing his drugs in gaudy pink, blue, and red paper. The manila paper formerly largely used for the cheaper goods, should not be used by elegant dispensers; such paper is admirably adapted to the wrapping of packages to be sent by mail or express, but it should not be seen wrapped around any product taken out of the drug store by the purchaser.

In place of string or rubber bands there has been lately introduced an attractive form of fastener in the shape of ribbon on which is imprinted the name of the firm. Although such ribbon is expensive, the use of it is good business, affording the pharmacist a convenient method of publicity. A more recent and inexpensive development is the use of gummed paper with the dispenser's imprint upon it. This is supplied in rolls which can be attached to a moistening device and the paper in widths of about an inch is drawn over the moistener, cut to the length desired by means of a sharp edge attached to the moistening apparatus, and then used to seal the package.

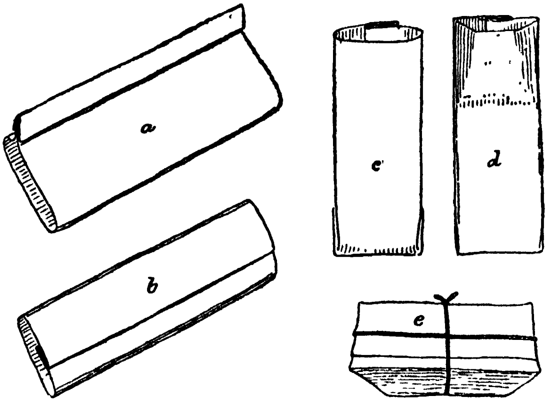


Fig. 200 —Wrapping package (see text).

To return to the subject of the dispensing of powders: if the powder contains deliquescent substances, the ordinary powder paper should not be used, as the moisture will soon penetrate to the ingredients and the paper will become wet. Such deliquescent powders should be wrapped in paraffin paper and then covered with tin-foil in order to prevent, as far as possible, atmospheric action.

The *powders of the Pharmacopœia* represent mixtures of the medicinal constituents not divided into specific doses, the only exception of this rule being Seidlitz powder.

Even as all the pharmacopœial liquids—such as tinctures and fluidextracts—are directed to be finished as bulk fluids of definite strength, so all official powders except Seidlitz powder are to be finished as bulk masses. In this way the pharmacopœial powders differ from such official solids as pills, lozenges, and suppositories, which are finished in the form of divided doses.

TABLE OF OFFICIAL POWDERS

Process	*Galenic preparations*	*Chemical preparations*
All by simple trituration. Finished in undivided masses.	Aromatic powder (N.F. VI).	Chiniofon powder.
	Aromatic powder of chalk (N.F. VI).	
	Compound chalk powder.	
	Compound powder of acetanilid (N.F. VI).	
	Compound powder of jalap (N.F. VI).	
	Compound powder of pancreatin (N.F. VI).	
	Compound powder of rhubarb (N.F. VI).	
	Compound powder of senna.	
	Compound powder of zinc sulfate (N.F. VI).	
	Powder of ipecac and opium.	
Finished in divided doses.	Compound effervescent powders.	

SPECIAL NOTES ON OFFICIAL POWDERS

PULVERES EFFERVESCENTES COMPOSITI—Compound Effervescent Powders

(Pulv. Eff. Co.—Pulvis Effervescens Compositus U.S.P. X, Seidlitz Powders)

The mixture in a blue paper weighs not less than 9.5 Gm. and not more than 10.5 Gm., and contains not less than 23 per cent and not more than 27 per cent of $NaHCO_3$, and not less than 73 per cent and not more than 78 per cent of $KNaC_4H_4O_6.4H_2O$. The white paper contains not less than 2 Gm. and not more than 2.4 Gm. of $H_2C_4H_4O_6$.

Storage.—Preserve in well-closed containers and in a dry place.

Condensed Recipe.

Triturate 30 Gm. sodium bicarbonate with 90 Gm. potassium and sodium tartrate, divide equally and wrap in 12 blue papers. Likewise, divide 26 Gm. powdered tartaric acid into 12 portions wrapping each in a white paper.

For assay of the sodium bicarbonate and of the potassium and sodium tartrate, and of the tartaric acid, see U.S.P., p. 308.

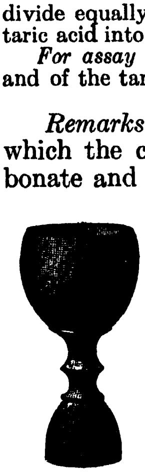


Fig. 201.—Seidlitz powder cup.

Remarks.—As mentioned previously, this is the one official powder in which the constituents are divided into special doses, the sodium bicarbonate and Rochelle salt being divided into 12 powders, wrapped in blue papers, while the tartaric acid is wrapped in white papers. In preparing Seidlitz powders the dividing of the powder is performed by using the so-called "Seidlitz powder cup" (Fig. 201); one of the cups is purported to hold the amount of Rochelle salt and sodium bicarbonate mixture, while the smaller cup is supposed to contain the amount of tartaric acid which is directed. These cups are used by taking a large quantity of the powdered substance on a sheet of paper, and filling the cup by pressing into the powdered mass, placing the cup over the powder paper, and emptying on the paper by a gentle tapping of the cup with a spatula. The use of such cups, however, does not necessarily mean a correct division of the chemicals, as the amount which the cup will hold depends entirely upon the pressure exerted. Some years since an investigator weighed Seidlitz powders obtained from the various stores throughout the country, and found that the weight of the Rochelle salt—sodium bicarbonate mixture put up in blue paper, ranged all the way from 133 to 251 grains, while the white paper contained] from 30 to 56 grains of tartaric acid. (Proper quantities, 155 and 33 grains respectively.)

For this reason it is wisest to weigh out the contents of each powder, a process more feasible than it seems.

The Rochelle salt—sodium bicarbonate mixture is obtainable in commerce under the name of *Seidlitz mixture,* and that sometimes at a price cheaper than the cost of the separate ingredients. There can be but one explanation of this fact: that such "cheap" Seidlitz mixture contains more than the 25 per cent of inexpensive sodium bicarbonate directed by the Pharmacopœia.

The effervescence occurring on mixing solutions of the contents of the blue and the white papers is due to liberation of carbon dioxide by the chemical action of the tartaric acid on the sodium bicarbonate. Details of this reaction will be found on p. 469.

A difference noted between the average home-made Seidlitz powder and that purchased in the market is the superior keeping quality of acid inclosed in the white papers of the purchased article. Tartaric acid is rather deliquescent, and the home-made "white papers" frequently begin to discolor (the paper wrapper becoming yellow), and not seldom become a moist mass. This trouble can be obviated by thoroughly drying the tartaric acid in an oven or by spreading in the sunshine on a dry day. The tartaric acid so dried will keep as well when wrapped as does that of the commercial Seidlitz powders.

Before leaving the subject of commercial Seidlitz powders reference must be made to an excellent grade found on the market, the subdivision and folding of which are performed on a special machine covered by patents.

Seidlitz powders are much esteemed as purgatives, the effervescence, when administered, masking the taste of Rochelle salts, which is the active ingredient. As is well known, Seidlitz powders are administered by dissolving the contents of the blue and of the white powder in separate glasses one third filled with water, mixing the two liquids, and drinking while effervescing; *not* by drinking the two liquids one after the other, as has been done more than once, with disastrous results.

Dose.—The contents of a white and of a blue paper, dissolved separately in about 1 fluidounce of water, and the solutions mixed.

PULVIS CHINIOFONI—Chiniofon Powder

This chemical mixture will be discussed in Part IV.

PULVIS CRETÆ COMPOSITUS—Compound Chalk Powder (Pulv. Cret. Co.)

Condensed Recipe.

Ingredients.—Prepared chalk, 30 Gm.: powdered acacia, 20 Gm.; powdered sucrose 50 Gm.

Manipulation.—Mix by simple trituration and sift. For details see U.S.P., p. 309.

Remarks.—Compound chalk powder, up to the present time, has been used almost exclusively in the manufacture of chalk mixture. *Chalk Mixture* (U.S.P. XI) is again made from this powder instead of directly from prepared chalk, as was the case in U.S.P. X (p. 279). Note that the compound powder is made from prepared chalk, not from precipitated chalk, for reasons given on p. 524.

Dose.—2 Gm. (30 grains).

PULVIS IPECACUANHÆ ET OPII—Powder of Ipecac and Opium

(**Pulv. Ipecac. et Opii.**—Dover's Powder, Pulvis Opii et Ipecacuanhæ Compositus P.I.)

Condensed Recipe.

Triturate 10 Gm. ipecac, in No. 80 powder, 10 Gm. powdered opium and 80 Gm. lactose in No. 20 powder until a fine uniform mixture results. For details see U.S.P., p. 310.

Remarks.—This is the popular *Dover's powder*, and contains 10 per cent ipecac, 10 per cent opium, and 80 per cent lactose. A microscopic description of the powder is given in the Pharmacopœia. This powder is classed as a narcotic and must be dispensed only on a properly written narcotic prescription.

Dose.—0.3 Gm. (5 grains).

PULVIS SENNÆ COMPOSITUS—Compound Powder of Senna

(**Pulv. Sen. Co.**—Compound Licorice Powder, Pulvis Glycyrrhizæ Compositus U.S.P. X)

Storage.—Preserve in air-tight containers.

Condensed Recipe.

Ingredients.—Powdered senna, 180 Gm.; powdered glycyrrhiza, 236 Gm.; washed sulfur, 80 Gm.; oil of fennel, 4 Gm.; sucrose, 500 Gm.

Manipulation.—Triturate the oil with some of the sucrose, add the rest of the ingredients, mix by trituration and run through a No. 80 sieve. For details see U.S.P., p. 310.

Remarks.—Compound powder of senna, formerly known as *compound powder of glycyrrhiza* is what is commonly called "compound licorice powder," and is an excellent remedy for costiveness. Note its ingredients, and that washed, not sublimed, sulfur is employed. The official title has been changed in order to name the most active ingredient in the title.

Dose.—4 Gm. (60 grains).

Pulvis Jalapæ Compositus (U.S.P. X; N.F. VI) or *Compound Powder of Jalap*, also called *pulvis purgans* is made by triturating together 35 Gm. powdered jalap and 65 Gm. potassium bitartrate. Its microscopy is described in the National Formulary. *Dose.*—2 Gm. (30 grains).

Pulvis Rhei Compositus (U.S.P. X; N.F. VI) or *Compound Powder of Rhubarb*, also known as *Gregory's powder* is made by triturating 25 Gm. powdered rhubarb with 10 Gm. powdered ginger, then adding 65 Gm. magnesium oxide. Compound powder of rhubarb or *rhubarb and magnesia* is yellow when first prepared, but turns pink on standing, due to the action of alkaline magnesia on the resins found in rhubarb. The N.F. monograph includes the microscopy of the powder. *Dose.*—2 Gm. (30 grains).

Pulvis Aromaticus (U.S.P. IX; N.F. VI) or *Aromatic Powder*, consists of cinnamon, ginger, cardamom seed, and nutmeg. As the latter is unstable in powdered form, the Formulary directs that it be freshly grated and then triturated with the other ingredients. The National Formulary gives a paragraph describing the microscopy of this powder. Aromatic powder is used chiefly to flavor other powdered substances, although it is of some value for relieving flatulence. *Dose.*—1 Gm. (15 grains).

Pulvis Morphinæ Compositus (U.S.P. VIII) or *Tully's powder*, was made by triturating 1.5 Gm. of morphine sulfate, with 33.5 Gm. of precipitated calcium carbonate; then with 32 Gm. of camphor previously pulverized by use of alcohol; and lastly with 33 Gm. of powdered glycyrrhiza. It enjoyed considerable popularity in New England, but under present-day narcotic legislation, its use is discouraged.

Dentifricium N.F. (N.F. VI) or N.F. *Dentifrice* now called *N.F. Tooth Powder* is a preparation introduced into N.F. V upon the suggestion of a committee of the national dental association. It contains hard soap, precipitated calcium carbonate, and soluble saccharin, and is flavored with oils of cinnamon, peppermint, and methyl salicylate.

DOSES OF OFFICIAL POWDERS

300 mg. (5 grains)	Compound powder of acetanilid (N.F. VI) and powder of ipecac and opium.
1 Gm. (15 grains)	Aromatic powder (N.F. VI) and chiniofon powder.
2 Gm. (30 grains)	Powders of chalk aromatic (N.F. VI), chalk compound, jalap compound (N.F. VI), and rhubarb compound (N.F. VI).
4 Gm. (1 drachm)	Compound powder of senna.
One set of two powders	Compound effervescent powders.

POWDERS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients. (figures show amount used in 100 Gm.)	Remarks.
Pulvis acetanilidi compositus.	Compound acetanilid powder.	Acetanilid, 70 Gm.; caffeine; sodium bicarbonate.	See p 782 *Dose.*—300 milligrams (5 grains).
Pulvis aromaticus	Aromatic Powder	. .. .	See p. 316.
Pulvis cretæ aromaticus	Aromatic powder of chalk.	Cinnamon; myristica; clove, cardamom seed, prepared chalk, sugar.	*Dose.*—2 Gm. (30 grains).
Pulvis jalapæ compositus.	Compound powder of jalap	Jalap, 35 Gm., potassium bitartrate.	*Dose.*—2 Gm. (30 grains).
Pulvis pancreatini compositus.	Peptonizing powder.	Pancreatin, 20 Gm.; sodium bicarbonate.	One and one-half Gm. are capable of peptonizing 500 cc. of fresh milk.
Pulvis rhei compositus.	Gregory's powder.	Rhubarb, 25 Gm ; magnesium oxide; ginger	*Dose.*—2 Gm. (30 grains).
Pulvis zinci sulfatis compositus	Compound powder of zinc sulfate.	Salicylic acid; phenol; eucalyptol; menthol; thymol; zinc sulfate, boric acid.	Antiseptic powder (N F V).

LABORATORY EXERCISES

POWDER FOLDING AND WRAPPING

Camphor	5 Gm. (powder with a few drops of alcohol)
Zinc oxide	5 Gm.

Triturate together in mortar, divide by eye into 12 papers, fold, put into box, and wrap box, making neat package.

Remarks.—*Powdering camphor* is an example of pulverization by intervention (p. 138).

Folding of Powder Papers.—Crease all papers, lay down evenly, and proceed as on p. 308.

Wrap box in paper neatly, as explained on p. 312.

The division of the powders can be secured accurately only by weighing each separately. In this case each powder should weigh—

$$\frac{5+5}{12} = \text{Gm., or } 0.83 \text{ Gm.}$$

The process is not difficult after one becomes expert at it. In this case divide by eye (see p. 307), and then prove the uncertainty of this plan by weighing three finished powders taken at random.

SPECIES

This represents a mixture of drugs, usually of vegetable origin, dispensed either in coarse powder or in a more or less roughly comminuted form. There is no official representative of this class, but the following were included in the National Formulary V.

Species Emollientes or *Emollient Cataplasm,* consisting of althea leaves; mallow leaves; melilot, matricaria and linseed.

Species Laxativæ or *St. Germain Tea,* consisting of senna; elder flowers; fennel; anise; and potassium bitartrate.

Species Pectorales or *Breast Tea,* consisting of althea; coltsfoot; glycyrrhiza; anise; mullein flowers; orris root.

TRITURATIONS

Triturations were suggested by similar preparations used in homeopathic practice. The Pharmacopœia gives a general formula calling for 10 per cent of the medicinal substance and 90 per cent of lactose.

TRITURATIONES—Triturations

Recipe.

Unless otherwise directed, Triturations are to be prepared according to the following formula:

The Substance	10 Gm.
Lactose, in moderately fine powder	90 Gm.
To make	100 Gm.

Weigh the medicinal substance and the lactose separately; then place the substance, previously reduced, if necessary, to a moderately fine powder, in a mortar; add about an equal measure of lactose, mix well by means of a spatula, and triturate the powders thoroughly together. Then add fresh portions of the lactose, from time to time, until the whole is added, and continue the trituration after each addition until the substance is intimately mixed with the lactose and reduced to a fine powder.

Remarks.—Note that the lactose must be added little by little.

Trituratio Elaterini (U.S.P. IX) or *Trituration of Elaterin*, is made by mixing 10 Gm. elaterin with 90 Gm. lactose. *Dose.*—0.03 Gm. (½ grain).

Homeopathic triturates are grouped into the classes "x" or dilutions one in 10; "c" or dilutions one in 100; and "m" or dilutions one in 1000. A dilution "2x" or "xx" is prepared by triturating one part of the drug with 9 parts of the diluent (making an "x" triturate) and then triturating one part of this "x" triturate with 9 parts of diluent. Ordinary mortals would consider this "2x" trituration clearly a 1 per cent preparation, the same as a "c" dilution, which is also certainly a 1 per cent trituration, but homeopaths insist that the differing manipulation makes the two products quite different. In passing it might be said that homeopathic tinctures "x" and "c" are prepared on a similar theory.

Hahnemann directed that in making 100 grains of triturate "c," 1 grain of the medicament be triturated successively with 3 times 33 grains of lactose and that six minutes be spent in trituration and four minutes in scraping the powder from the mortar each time the 33 grains of diluent is added. Modern homeopaths defend excessive triturations and excessive dilutions by citing the importance of the infinitely small in modern physics.

OLEOSACCHARA

This is a class of preparations which, as suggested by the name, "oleum" and "saccharum," represents sucrose (sugar) which has been flavored with some aromatic oil. Such oleosacchara or *oil sugars* are quite popular in Germany, where they are used as diluents in the preparing of many powders. They are made by placing the sucrose (sugar) in a mortar, adding the volatile oil, and triturating until the oil is thoroughly divided by the sucrose (sugar).

The National Formulary gives a general formula for the manufacture of them, directing that they be made by triturating 2 cc. of the prescribed volatile oil with 100 Gm. of powdered sucrose (sugar). Those mostly prescribed are the oil-sugar of anise, of fennel, and of peppermint.

ADMINISTRATION OF POWDERS

A medicated powder is usually administered by placing the proper dose, if small, on the tongue, and then swallowing same in a draft of water. In cases of intensely bitter substances, such administration is scarcely short of inhuman; hence efforts have been made to prevent the bitter substance from coming into contact with the palate by enveloping the drug in a tasteless inert tissue. Such is the origin of the now widely popular cachets and capsules.

CACHETS

The original cachets were wafers made of flour, identical with the consecrated bread used in the sacramental service of the Roman Catholic Church.

These wafer papers were made of pure flour paste, rolled between hot greased rollers, thus driving out the moisture and leaving the paste in a thin, translucent sheet. Such wafer papers are put on the market in either round or square forms, and in dispensing powders in such wafers the wafer is placed in the bowl of a tablespoon which has been previously moistened with about a half teaspoonful of water. After the wafer has been in the spoon for about a minute, the outer surface will become uniformly moistened, and into the interior of the wafer is then placed the powder, the wafer edges folded over while still in the spoon, thus making a three-cornered or nearly round package. The folded wafer is then quickly immersed in the water, placed in the mouth, and swallowed by aid of a draft of water.

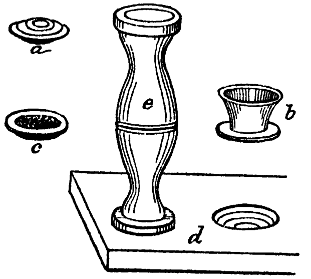


Fig. 202.—Limousin's cachet: *a*, Finished cachet; *b*, cachet funnel (enlarged); *c*, cachet containing powder; *d*, portion of cachet board with (*e*) presser and moistener.

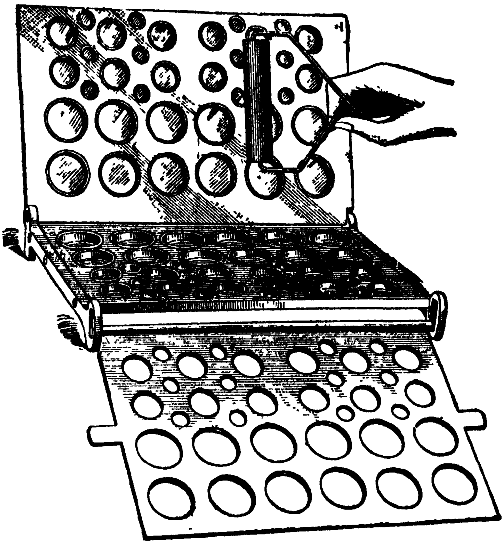


Fig. 203.—Conseal filling apparatus.

As can be imagined, the administration of powders in wafer papers is exceedingly crude, and it was not lông before attempts were made to use the same principle in a more elegant way. This was accomplished by Limousin, who introduced wafers in the form of concave halves, each half being provided with a flange, which can be moistened and pressed to the other half, thus securing adhesion. (See Fig. 202.) The powder is placed on one half and the other half moistened with water along its flange, placed on the half containing the powder, and in this way a tightly sealed elliptic disk, containing powder on the interior, is obtained. Limousin introduced, along with this cachet, elaborate machinery for the sealing of same, and such a mode for the administration of powders is popular in European countries.

Conseals are a very slight variation of the original Limousin wafer, the shape of them being the same, but the filling apparatus is simpler. The appended sketches fully explain the various portions of the sealing apparatus, so extended comment is unnecessary (Fig. 203).

CAPSULES

Capsules are hemispheric or ovoid shells of gelatin, and are used for the administration of powders, masses, or liquids. According to the quantity of glycerin contained in a capsule mass, the capsules are hard or soft. Hard capsules usually have been the form shown in the appended figures, and consist of a shell and a cover (cap) (*a* and *b* in Fig. 204). Soft capsules are generally shaped like a flask, as shown in Figs. 205 and 206, and these are sealed by dropping a bit of melted capsule mass on the orifice. The capsules are manufactured by dipping the appropriate mold into the mass, made by dissolving gelatin in a mixture of hot water and glycerin in such proportions that the mass is fluid when heated on the water bath and solid when cold. Into the melted mass the appropriate mold, made of bone or ivory, is dipped (Fig. 207), with the result of coating each mold with a layer of gelatin. When the molds are taken from the molten mass and placed in a cool place, they rapidly solidify, and the solid dry capsules are stripped from the molds by hand.

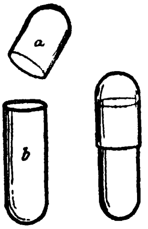
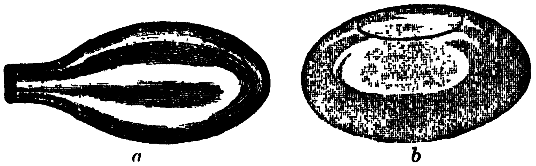


Fig 204.—Gelatin capsule: *a*, The cap; *b*, the body.



Figs. 205, 206.—Soft capsules: *a*, Unfilled; *b*, filled.

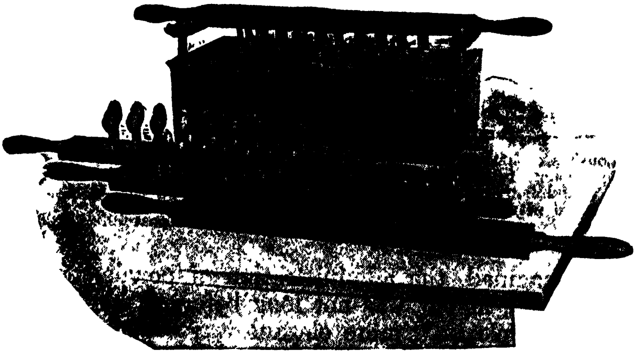


Fig. 207.—Stokes' capsule mold.

Capsules are now manufactured on the elaborate machine shown in Fig. 208. This is operated by electricity and contains pins, both for the shell and the cap, of noncorrosive phosphor bronze on which the capsules are molded. These pins are on bars, which are on endless chains and are dipped into the melted gelatin solution. When the capsule parts have dried upon the pins, they are mechanically trimmed, the caps are fitted upon the shells and the finished capsules are blown into a receptacle by compressed air.

The first capsules were prepared by Mothes in 1833, while the two-piece shell capsule now so largely used was patented by Murdoch in 1848.

Soft capsules are not used to the extent that they should be by the retail pharmacist. They are usually employed for the administration of liquids, and can be secured of sizes ranging, in capacity, from 1 fluidrachm to ½ fluidounce. The form of soft capsule particularly adapted for dispensing by the pharmacist is that made by the Merz Capsule Co., the firm having also devised an ingenious filler, shown in Fig. 209.

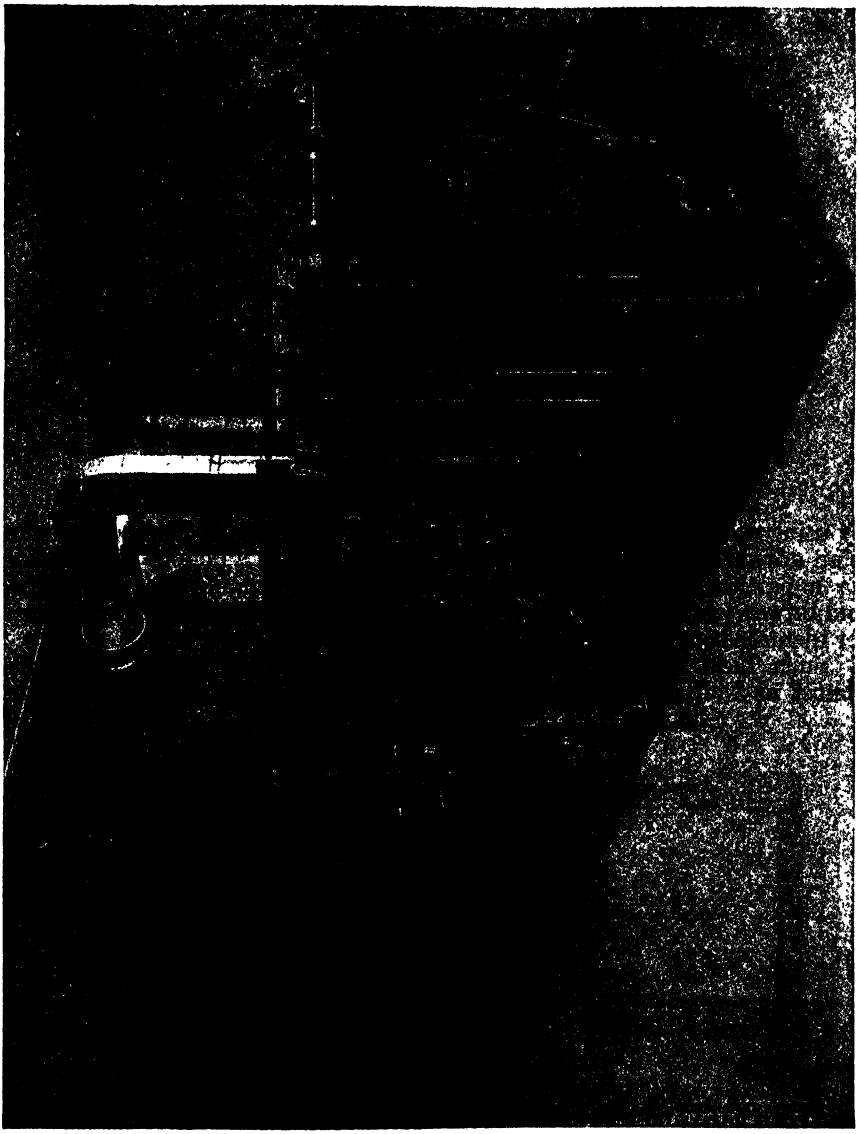


Fig. 208.—Colton capsule machine.

Hard capsules have become a necessity in every drug store, and, in fact, in almost every household. A typical recipe for the material from which they are made calls for gelatin, 8 parts; sugar, 8 parts; acacia, 1 part; and water, 8 parts. They range in size from the capacity of 0.12 cc. (No. 5) to 0.9 cc. (No. 00); the weight of the medicine they contain, of course, depending on the specific gravity of the substance, and in case of a powder, on the degree of packing. A table of the average capacity of such capsules for well-known solids is found on the boxes of the best known brands of capsules. Hard capsules are now made in various colors by using a harmless dye in the gelatin batch. The use of colored capsules is an advantage when a physician desires to indicate a change in medicine for a particular patient. The principal colors available are pink, blue, and brown. Many manufacturers also imprint capsules of their specialties for identification.

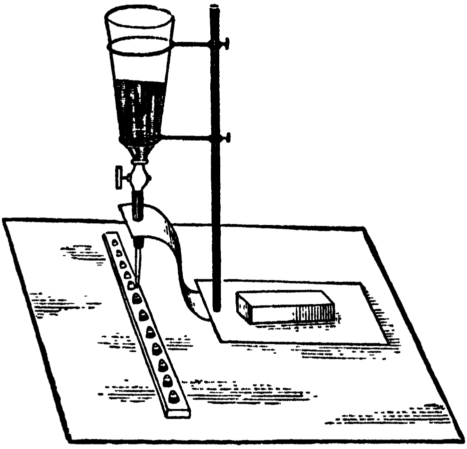


Fig. 209.—Merz capsule filler.

Such hard capsules can be used for the administration of liquids almost as well as can soft capsules, it being scarcely necessary to state that both hard and soft capsules can be used for holding only those liquids which will not dissolve nor soften gelatin. Hence the dispensing of liquids in capsules is limited largely to fixed and volatile oils.

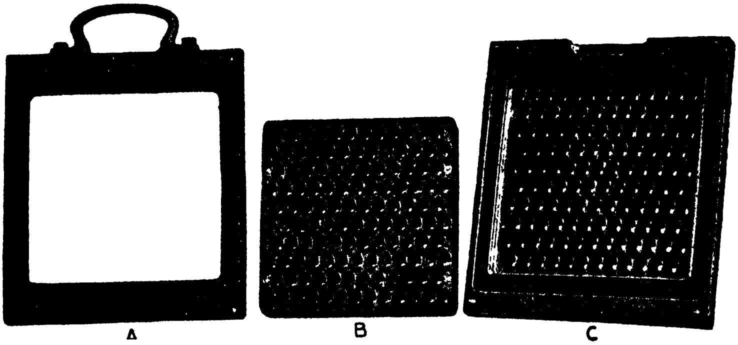


Fig. 210.—Colton globule mold.

In dispensing oils in hard capsules, the oil is introduced into the capsule, by means of a dropper or, better, from a burette; the capsule is then sealed by moistening sufficiently to cause the cap to adhere to the shell, making a liquid-tight joint.

Two ways of sealing capsules have been suggested, the first by moistening the upper edge of each filled shell with water by means of a delicate camel's-hair pencil which is fastened to the little finger by means of a wire. This process is by no means so satisfactory as the one devised by L. C. Hopp, which consists of placing the caps with the open end down on a flat dish or tin box cover, into which a minute quantity of diluted alcohol is poured. After letting the caps remain in the diluted alcohol for a minute or two they will have absorbed just enough water to make them adhere and yet not enough to make them soft. After the caps are fitted into the shells, all that is necessary is to rotate that portion of the capsule where the seal has been made between the fingers for a few seconds. Such finished hard capsules, containing oils, should, however, before dispensing, be placed on a filter paper to see if there is any leak. Those that leak should, of course, be rejected.

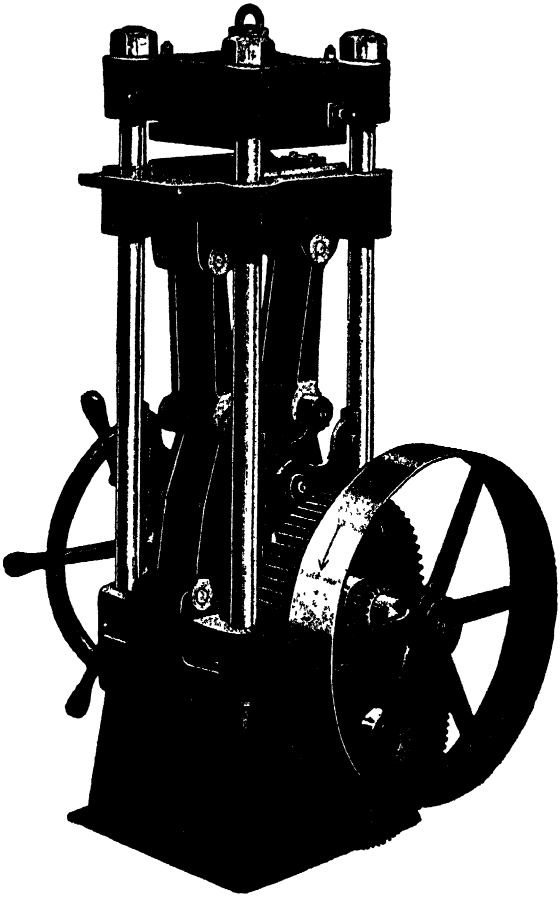


Fig. 211.—Colton 3 toggle globule press.

Pearls or globules are gelatin capsules prepared by placing sheets of gelatin softened with glycerin upon tin-coated molds of steel 9 inches square and provided with hemispherical depressions. The soft gelatin sheets are fitted to two such molds, the liquid medicine is poured between the gelatin sheets which are then made to adhere by use of a powerful press. After pressing the circular or oval "pearls" are separated from the superfluous gelatin mass, are washed in acetone and are then dried externally and packed (Figs. 210 and 211).

In dispensing solid drugs in capsules recourse was formerly had to the working of the solid into a pill mass, dividing the mass into pieces, as in making pills, rolling these pieces into cylinders, and inserting the same into the capsules. Such method of dispensing solids is, however, no longer considered good form, and the pharmacist should always dispense capsules containing the drugs in powder unless otherwise directed by the physician, or, which means the same thing, unless the physician prescribes some semisolid or liquid along with the powdered drug.

Capsules afford a means for dispensing powders in the most readily soluble form, and such capsules containing the powders are much better than any class of pills yet devised, not even excepting the much vaunted friable pills. Such capsules contain nothing but the powders surrounded by a gelatin shell, and the moment they enter the stomach the gelatin dissolves, thus throwing the powders into the stomach in absorbable form. It, therefore, behooves the progressive pharmacist to emphasize to physicians his ability to dispense such capsules and to add the fact that this form of administration of drugs is superior to any form of ready-made pill.

The filling of capsules with powders can be accomplished by placing the mixture of powders on a clean sheet of paper and pressing the shell into the mixture of the powders, when it will gradually fill by gentle pressure. In order to obtain the exact amount of powder directed for each dose, each filled capsule should be weighed, and this is an easy matter by having on one scale the weight plus the empty capsule, and throwing the filled capsule on the other pan. If the exact quantity is not in, a little more pressure will bring the sufficient weight, and in case of an excess, a slight tapping of the inverted capsule will throw out the surplus. The filled capsule must be carefully cleaned from adhering drug. This can be done by wiping each capsule with a clean dry cloth or, better, by use of the Remington capsule cleaner (Fig. 212).

Fig. 212.—Remington capsule cleaner.

This consists of a metallic box with cover containing an interior perforated plate. Granular sugar is poured into the box and the filled capsules are then shaken with the sugar. Inverting the box, the sugar sifts out leaving the clean capsules ready for dispensing.

Eckles finds that powders can be more readily filled into capsules if the powder is first triturated with olive oil (1 drop per capsule).

There have been a large number of special apparatus for capsule filling placed on the market. Among these, the following may be cited.

The Ihrig capsule filler is shown in Fig. 213. It consists of a metal base with a movable plate, having perforations to hold the various sized capsules, which can be raised out of the perforations, in this case by means of a thumb screw. The perforations on the plate are arranged to fill the five sizes of capsules, each set of the different sizes of the perforations

Fig. 213.—Ihrig capsule filler.

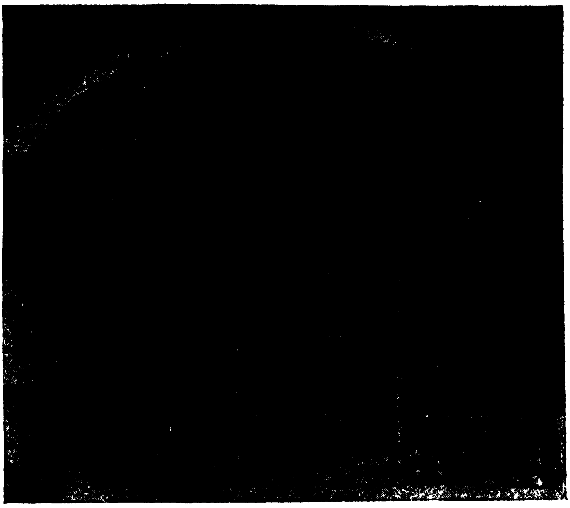


Fig. 214.—Remington automatic capsule filler.

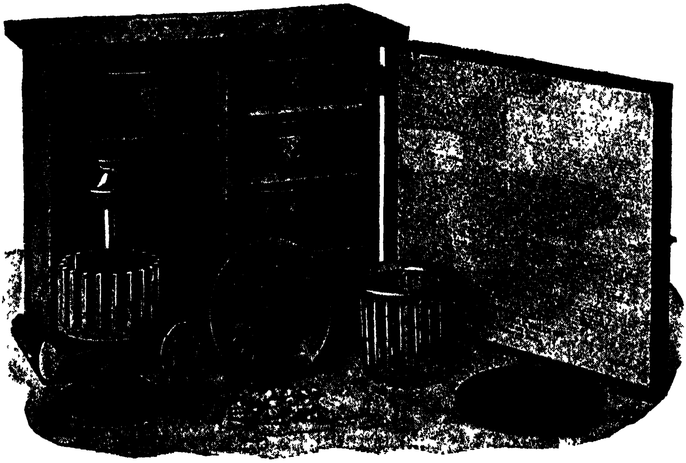


Fig. 215.—The Eastman capsule filler.

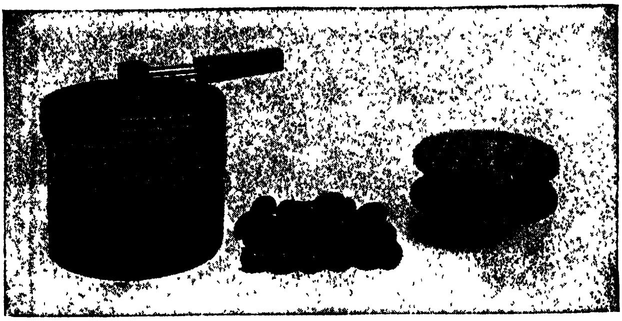


Fig. 216.—Lascoff capsule filler.

Fig. 217.—Lascoff capsule filler.

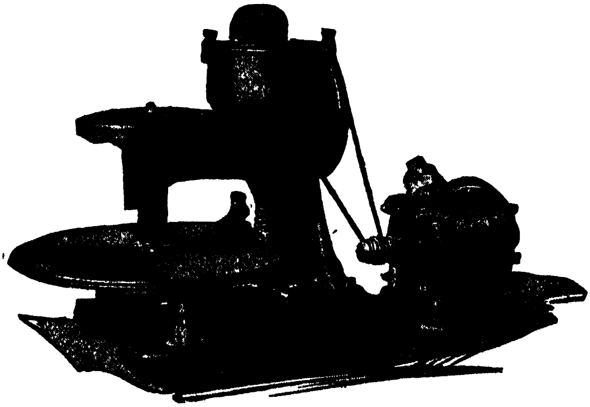


Fig. 218.—Stokes' power capsule filler.

being arranged in the portion of the plate by itself. When the apparatus is used, the shell of the capsule should be on a perfect level with the top of the plate, or a trifle below the surface. When the requisite amount of capsules have been placed in the plate, the powder is poured on that part of the plate and gradually forced into the shell of the capsule by the use of a spatula, the last portion of the work being aided by a punch which fits into three capsules at one time. When all the capsules have been filled, the thumb screw is turned so that the plate is lowered against the pegs that project from the base, the plugs then pass into the perforations of the plate, thus pushing the shells above the surface of the plate. A cap is then placed on each shell, and the sealed capsule removed from the plate.

Among recent types of capsule fillers we find the Remington (Fig. 214) and the Eastman (Fig. 215). The Lascoff apparatus (Figs. 216 and 217) is designed to fill soft capsules with liquid, while the Stokes power capsule filler (Fig. 218) will fill at the rate of 30 capsules per minute.

GRANULAR EFFERVESCENT SALTS

This class of preparations consists of powdered chemicals finished in a granular form. These effervescent salts are quite different from the true granular salts, such as granulated ferrous sulfate (p. 565) inasmuch as they are devoid of crystalline property, and are called "granulated," because consisting of the chemical in uniform and small particles.

Granular effervescent salts always contain tartaric and citric acid and some carbonate, so that when mixed with water copious evolution of carbon dioxide gas occurs (p. 469). Here need it only be said that these preparations are made by mixing the active chemical with the acid and the carbonate, moistening with alcohol, and running the moist mass through a coarse sieve, whereby it separates into small and regular particles. The reason the mass is moistened with alcohol is that alcohol renders it sticky without producing the chemical action between the acid and the carbonate which would result were they moistened with water. For the same reasons these preparations must be kept in tightly-stoppered bottles to prevent contact with moist air, which would soon render them no longer effervescent. These salts can also be granulated by softening the mass by heat of a water bath and passing the soft mass through a sieve.

In manufacturing granular effervescent salts on a large scale, the ingredients are combined in an enamelled mixer, the mixed acids (tartaric, 1 part; citric, 2 parts) are added last and the well mixed powdered mass is then softened either in enamelled steam pans or on glass plates warmed in an appropriate oven. When softened, the mass is forced through a 6 to 8 mesh mechanical sifter, the sifted granules being dried either on a belt dryer or in a vacuum dryer. An essential to large-scale manufacture of these salts is a work room full of *dried* air and kept at a temperature of 110° to 120° F.

The National Formulary, under the title *Salia Effervescentia*, gives a monograph on effervescent salts that is worth careful reading.

The Formulary also recognizes the following individual effervescent salts:

Sal Carolinum Factitium Effervescens, or *Effervescent Artificial Carlsbad Salt.*

Sal Kissingense Factitium Effervescens, or *Effervescent Artificial Kissingen Salt.*

Sal Lithii Citratis Effervescens, or *Effervescent Salt of Lithium Citrate.*

Sal Magnesii Sulfatis Effervescens, or *Effervescent Magnesium Sulfate.*

Sal Potassii Bromidi Effervescens Compositum, or *Compound Effervescent Salt of Potassium Bromide.*

Sal Vichyanum Factitium Effervescens, or *Effervescent Artificial Vichy Salt.*

The present Pharmacopœia recognizes two effervescent salts; *effervescent potassium citrate* (p. 469) and *effervescent sodium phosphate* (p. 490).

SCALED PREPARATIONS

This represents another class consisting of chemicals in a special form; that is, in the form of attractive noncrystalline scales. These are made by evaporating a solution of the chemical or chemicals to a syrup and then pouring the syrup on a hard smooth surface, such as a pane of glass or a porcelain pill tile. Upon drying, the chemical peels off in scales. In this way the scale salts of iron (p. 574) and of bismuth (p. 579) as well as scale pepsin (p. 954) are prepared.

BIBLIOGRAPHY

Powders.—(Preparation) Rice, Am. Dr., 14, 1885, 8 and 124; Anon., Dr. Circ., 73, 1929, 493; Stedem, Dr. Bull., 52, Mch., 1930, 12. (Dispensing) Anon., Ch. and Dr., 41, 1892, 155. (James') Coxe, A.J.P., 5, 1833, 270; Robinson, A.J.P., 6, 1834, 282; Unzicker, Dr. Circ., 9, 1865, 107; Anon., Ch. and Dr., 10, 1924, 508. (Seidlitz) Thompson, A.J.P., 68, 1896, 337; Culbreth, Dr. Circ., 41, 1897, 274; Anon., Pract. Dr., 48, Dec., 1930, 34. (Dover's) Anon., Nat. Dr., 40, 1910, 280; Dixon, Midland Drug, 48, 1914, 34. (Tully's) Wood, A.J.P., 51, 1879, 224.

Triturations.—Witte, Essentials in Pharmaceutics, 1902, 24; Kleiner, C. A., 19, 1925, 2833.

Wafer Papers and Cachets.—Limousin, Am. Dr., 16, 1887, 145.

Conseals.—O'Connor, Spatula, 26, 1920, 129.

Capsules.—(History) Garot, Jl. de ph., 24, 1838, 78; Planten, Art of Capsulating, 1909; Feldhaus, Ch. Zt., 36, 1912, 74. (Manufacture) Carrier, Bull. Pharm., 28, 1914, 204; Grosh, Merck's Rep., 22, 1913, 57; F. H., Am. Dr., 55, 1909, 146; Hopp, A.Ph.A., 51, 1903, 435; Alpers, A.Ph.A., 44, 1896, 175; Emanuel, Am. Dr., 56, 1910, 193; Forret, Merck's Rep., 15, 1906, 100; Robin, Ph. Era, 35, 1906, 50; Lascoff, Year Book, A.Ph.A., 4, 1915, 23; Harmer, Proc. Pa. Pharm. Assn., 40, 1917, 239; Marsh, Sci. Am., 117, 1917, 194. (Filling and cleaning) Stedem. Dr. Bull., 52, Apr., 1930, 12; Eckels, So. Pharm. Jl., 18, 1926, 310; Lee, Jl. A.Ph.A., 24, 1935, 469. (Enteric) DuMez, Jl. A.Ph.A., 10, 1921, 372.

Globules or Pearls.—White, Proc. Pa.P.A., 43, 1920, 282.

Effervescent Salts.—White, Jl. A.Ph.A., 10, 1921, 609; Simon, Ph. Jl., 107, 1921, 519.

Scale Salts.—Simon, Ph. Jl., 107, 1921, 519.

CHAPTER XIX

MASSES, CONFECTIONS, AND PILLS

MASSES

Masses are combinations of medicines worked up with enough liquid to make solids of sufficient plasticity to roll into pills.

The manufacture of the official masses is a matter of little difficulty, as in each recipe the quantity of liquid prescribed is sufficient to make a mass of the required plasticity. The manufacture of dry powders into pill masses is a matter requiring skill, and will be fully dealt with when considering pills.

There are but two masses recognized by the Pharmacopœia, one of them is a chemical preparation (mass of ferrous carbonate), the other, a galenic (mass of mercury). Mass of copaiba was recognized in the Pharmacopœia of 1890, but was dropped at the eighth revision.

SPECIAL NOTES ON OFFICIAL MASSES

MASSA FERRI CARBONATIS—Mass of Ferrous Carbonate

This preparation, commonly called *Vallet's mass*, can best be studied among the preparations of iron in Part III.

MASSA HYDRARGYRI—Mass of Mercury

Mass of mercury contains not less than 32 per cent and not more than 34 per cent of Hg.

Recipe and details of manufacture will be found below.

Remarks.—Mass of mercury is the well-known "blue mass," or blue pill and its manufacture by hand is a matter demanding skill and labor. The tendency of the mercury to run together and to form globules is well known, and in making the mass we aim to break the mercury into globules so small that they are not even visible under the glass magnifying ten diameters. These minute globules are coated with something that will prevent them from running together, and this process of division, called "extinguishing," is accomplished in the mass by triturating the mercury with oleate of mercury and honey, and then adding glycerin, glycyrrhiza, and althea. Note that the present Pharmacopœia provides an assay of the mercury content of this mass. (See Part V.)

Dose.—0.2 Gm. (3 grains).

LABORATORY EXERCISE

MAKE BLUE MASS

Recipe.—	Mercury	3.3 Gm.
	Oleate of mercury	0.1 Gm.
	Glycyrrhiza, in No. 80 powder	1.0 Gm.
	Althea, in No. 80 powder	1.5 Gm.
	Glycerin	0.9 Gm.
	Honey	3.2 Gm.
	To make	10 Gm.

Triturate the mercury with the oleate of mercury, then add a part of the honey and triturate the mixture until globules of mercury are no longer visible under a lens magnifying at least ten diameters. Add the remainder of the honey and the glycerin and althea, and continue the trituration until the mass is homogeneous. Keep the product in well-closed containers.

Remarks on Process.—*Triturate the mercury with the oleate of mercury and honey in a mortar until extinguished*—that is, until no mercury globules are seen and a thin gray paste results. If trituration is stopped, however, the globules will run together.

Add the rest of the honey, the glycerin and the powdered drugs and then triturate vigorously. This has the effect of coating each globule of mercury with the powder, thus preventing one from running into the other.

Triturate until no globules are seen under glass magnifying ten diameters—that is, making things look ten times their real size. To accomplish this usually takes a half hour's trituration.

Massa Copaibæ (U.S.P. 1890; N.F. V) or *Solidified Copaiba*, is interesting because 94 parts of the liquid, copaiba, are directed to be solidified by trituration with 6 parts of magnesia; this solidification being due to the formation of the magnesium salt of copaibic acid found in the oleoresin. (See p. 865.)

Every specimen of copaiba, however, does not solidify on treatment with magnesia nor is it fair to claim that such copaiba is not up to Pharmacopœial requirements.

The copaibas of commerce are divided into two groups—the ordinary and the solidifiable; and in preparing the mass of copaiba the latter should be used exclusively.

It is claimed, however, that much of the solidifiable copaiba of commerce is made so by addition of ordinary rosin.

There are several proprietary articles on the market under the name of extract of copaiba which closely resemble the official mass. They, however, are usually solidified by trituration with the cheaper alkali, lime.

By reason of the solidification of copaiba with magnesia, that substance is indicated as the excipient in making pills containing copaiba.

CONFECTIONS

Confections are a class of preparations in which medicinal substances are combined with saccharine substances, like jellies or the pulp of fruits. Confections are also called *conserves* and *electuaries*, the word confection being derived from the Latin "*conficio*," meaning to make up. In the days of ancient pharmacy confections were a favorite mode of administration of medicines, since nearly all medicines then administered were nauseous and disgusting, and in order to render them more palatable, attempts were made to cover the unpleasant features by combining them with sweet substances.

In ancient times a large number of confections were used, a famous one of which was the *confection of Damocratis*, which contained from 50 to 100 ingredients.

The long line of confections of the olden days have so fallen into disuse, that during the ninth Pharmacopœial revision the two surviving representatives of this class, confection of rose and confection of senna, were deleted.

Confectio Rosæ (U.S.P. VIII; N.F. V) is prepared by making a mass from red rose, sucrose (sugar), honey and stronger rose water. It has no medicinal value but is a pleasant pill excipient.

Confectio Sennæ (U.S.P. VIII; N.F. V) is made by digesting cassia fistula, tamarind, prune and fig with water, rubbing the pulpy mass first through a sieve and then through muslin, adding sucrose (sugar) to the pulp thus strained after which it is evaporated to a definite weight. To this masslike product, powdered senna (10 per cent) and oil of coriander are added.

Confection of senna is an admirable preparation furnishing an efficient laxative in a palatable form. A large number of preparations of similar composition have been put on the market as patent medicines, the semisolid mass being broken in pieces and eaten when required.

The best known of this class of patents is *Tamar Indienne*. Of late years even the proprietary articles have fallen into disuse, while the formerly official confection of senna is rarely prescribed by physicians. *Dose.*—4 Gm. (60 grains).

PILLS

Pills are spheric, globular, or lenticular masses, each containing a definite dose of medicinal substances, administered by swallowing whole.

The manufacture of pills, while formerly one of the most important branches of pharmacy, is becoming a lost art, due to the introduction of machinery which can perform the work with much greater expedition and also to the much greater use of compressed tablets and capsules. Since extemporaneously prepared pills are usually better than the manufactured ones, by reason of the greater solubility, it is important that all the details of their preparations be fully understood.

The manufacture of pills by hand can be roughly divided into three parts: first, making the mass; second, dividing the mass; third, rolling the pills.

Making the Mass.—In performing this operation the medicinal ingredients are, after careful trituration until uniform subdivision is obtained, worked into that plastic semisolid form known as a mass. This mass should possess four requirements if it be ideal: first, it should be sufficiently *adhesive* that it can be rolled without falling to pieces; second, it should be *firm* enough to retain its shape when rolled; third, it should be *plastic* enough to be easily rolled—that is, not so hard as to make the rolling a matter of considerable labor and yet not so soft that the finished pills are flattened during drying; fourth, and most important of all, the pill mass should be *soluble;* that is, on being introduced into the stomach it should disintegrate within a reasonable time.

In making a pill mass we usually have recourse to the excipient, and this excipient is different from what we usually and narrowly conceive it to be. Ordinarily, we consider it as a sticky mass with which we "paste" up a solid into pill form. In the broad sense, however, the term applies with equal force to those substances with which we solidify liquids into pill form—like the magnesia used to solidify copaiba.

Among the excipients used in making pharmaceutic pills are *water, sulfuric acid, syrup, syrup of acacia, mucilage of acacia, glycerin, glucose, honey, glycerite of tragacanth, extract of gentian, bread crumbs, powdered glycyrrhiza, powdered althea, soap, resin cerate, petroleum mass.*

Water is used for making pills only when the pill mass contains some ingredient, which, when moistened, forms an excipient. Thus, if the mixed powder contains adhesive substances, such as acacia or soap, the addition of a few drops of water and working up of the mixture will result in a pliable mass. In such cases, however, the action is the same as if mucilage of acacia or soap and water were used.

Sulfuric acid, either concentrated or in the form of aromatic sulfuric acid, is sometimes used as an excipient in the manufacture of pills of quinine sulfate. When the acid is added to this chemical it forms a soft and comparatively plastic mass of quinine bisulfate, which can be divided into pills if the mass is worked rapidly. Such method of dispensing quinine sulfate was very largely employed in the South in former years, but is now falling into disuse.

Syrup is used for certain forms of pills, but is scarcely efficient unless there is present in the mixed powder some gummy substance.

Syrup of acacia would be an excellent excipient were it not for the fact that the finished product, when dry, is usually so hard as to seriously impair its solubility.

Mucilage of acacia has the same advantages and disadvantages of syrup of acacia.

Glycerin is rather extensively used in making the pills of the alkaloids, such as quinine sulfate. It has never been found satisfactory in the hands of the writer by reason of its lack of adhesiveness. One advantage of glycerin as an excipient is that its hygroscopic character keeps the pill soft and thus soluble for quite a while.

Glucose is very largely used as an excipient, being both adhesive and plastic.

Honey is sometimes used, but it has no advantage over glucose, of which it largely consists, and possesses the very decided disadvantage of imparting to the mass a slightly brownish tint.

Glycerite of tragacanth, consisting of 3 drachms of powdered tragacanth, 3 fluidounces of glycerin, and ½ fluidounce of water, has always been the writer's favorite excipient, it yielding a mass both plastic and adhesive and firm. Similar results can be gained by the use of the official *glycerite of starch.*

Extract of gentian has been prescribed as an excipient and is valuable in tonic pills. *It should, however, never be used as an excipient unless so directed by the physician.* In the first place, gentian has definite medicinal properties, and the pharmacist should never add to a prescription any medicine other than that directed in the recipe. Another point is that it possesses a brownish tint, and thus discolors the pill mass. This is of no concern if the ingredients of the mass are of dark color; but it is a dictum in good pharmacy, that colorless ingredients should be made up into a colorless mass.

Bread crumb is used for holding liquids, such as volatile oils, in the plastic form. Thus, were pill of croton oil directed, the crumb of bread would be indicated. *Magnesia* is used in a similar way with the liquids on which it exerts a solidifying action. Thus, copaiba directed in pills should be massed by means of magnesia (p. 329) and this is also true of Venice turpentine.

Soap is used in persuading resinous substances to assume the plastic form. Thus, pills containing aloes are made plastic and adhesive by the addition of soap.

Yeast extract is now highly recommended as a general excipient by German pharmacists. It has been put upon the market under the name, *cenomassa zyma.*

The *rosin cerate* and *petroleum mass* are used as excipients for pills containing certain oxidizing chemicals, such as potassium permanganate, chromic acid, and silver oxide. For this purpose a petroleum mass consisting of kaolin, 3 parts; paraffin, 1 part; and petrolatum, 3 parts, can be used to advantage. Fantus favors the Marshall excipient mixture of 2 parts of kaolin and 1 part of anhydrous sodium sulfate.

The following drugs, frequently prescribed in pill form, require special manipulation:

Volatile oils can best be massed with sodium stearate, made from hardened cotton seed oil. If a softer soap is used, the soft mass may be stiffened by addition of fibrous material such as powdered quassia.

Creosote, or *guaiacol,* or other oily liquids may be massed by diluting with an absorbent powder like glycyrrhiza or althea, and massing with ordinary excipient. From such pills, however, the oils gradually ooze out, and the best way is to inclose the mass in capsules. T. M. Pratt found that by rubbing the oil with acacia, then with the diluting powders, and then with excipient, the oil is partially emulsified and the "sweating" is prevented.

Heavy salts, like *bismuth subnitrate, calomel,* or *sodium bicarbonate,* can be massed with glycerite of tragacanth. If desirable, a small quantity of powdered elm bark may be added.

Bismuth subnitrate and *sodium bicarbonate* when massed together swell and disintegrate, due to liberation of carbon dioxide. The powders should be moistened first with water and permitted to stand, until the reaction is over (one to three hours); then massed with glycerite of tragacanth. Kern finds that pills containing ergotin and sodium bicarbonate swell and disintegrate in a similar fashion.

Potassium iodide can be massed by adding to each 0.20 Gm. of the salt, starch 0.04 Gm.; powdered acacia, 0.08 Gm.; calcined magnesia, 0.10 Gm.; the excipient used being glycerin, 20 parts; syrup, 50 parts and alcohol, 30 parts.

The making of a pill mass is performed by thoroughly blending the powders by triturating in a mortar, adding the necessary quantity of excipient, and working the mixture with a pestle until a plastic mass results. (For details of the process see p. 342.) In modern pharmacy the mass-making apparatus range from a small pill mortar to a huge mixing machine (Fig. 219). The making of a successful pill mass is a matter of practice, and depends largely on the adding of the exact quantity of excipient when first starting the kneading. This really explains the psychology of the "favorite excipient," it being the writer's experience that the old-time pharmacist held as firmly to his pet excipient as he did to his political creed. The reason for this is that the individual has mastered the peculiarities of this special excipient, and such excipient is in his case the best that he can use, inasmuch as he has learned by intuition the exact amount required for each pill mass. Hence, unless the favorite excipient possesses marked defects, such as rendering the pills insoluble or the like, or bringing into the mass a medicinal effect not expected by physicians, no attempt should be made to wean a pharmacist from his favorite excipient.

Dividing the Mass.—When the mass has become sufficiently worked, that is, when the pressing of the pestle is sufficient to enable the mass to be rolled from the side of the mortar, it is then rolled into cylinders and divided either on the pill tile or by means of the pill cutter. The details of the use of a pill tile, both in working up the mass and also in dividing the same, is fully described on p. 342 and it is necessary here only to insert a picture of the apparatus (Fig. 220), which is made of porcelain or glass, with the painted graduations burnt in during the process of glazing of the porcelain or etched into the glass. In rolling out the pill mass into cylinders a spatula is used or, what is preferable, a flat board shaped like a paddle. As mentioned on p. 342, the pill tile should be carefully dusted with the appropriate dusting powder.

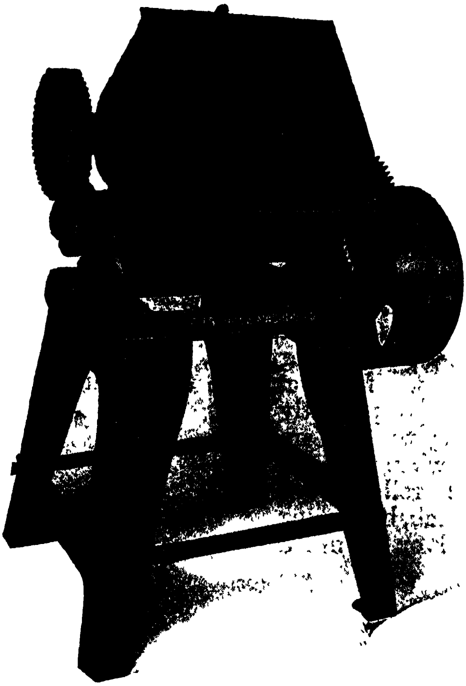


Fig. 219.—Stokes' mass mixer No. 20.

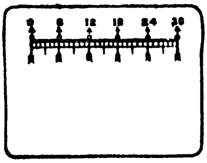


Fig. 220.—Pill tile.

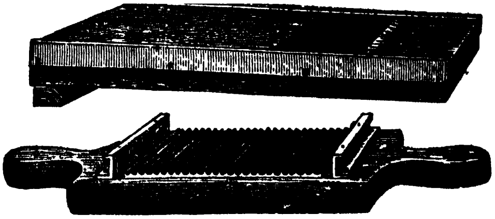


Fig. 221.—Pill-cutting machine.

As to pill-cutting machines, these usually consist of brass-bound walnut boards, holding at one end a brass mold, which is divided into a definite number of perfectly uniform hemispheric concave grooves. Working on this is a cutter, which consists of a narrow piece of walnut, provided at each end with stable handles, having attached to one side a brass plate with hemispheric grooves, exactly fitting those on the other part of the apparatus. A set of brass rollers, worked on the brass bands of the sides of the plate, completes the cutter (Fig. 221). In using such a machine the cylinder is placed on the wooden part of the board and rolled out, preferably with a wooden paddle, rather than with the back of cutter, to a length including the number of grooves representing the number of pills desired. The cylindric pill mass is then placed on the grooves of the machine, and the grooves of the cutters are then brought down upon it, thus dividing the cylinder into the number of segments desired. If the diameter of the cylinder exactly coincides with the diameter of the grooves, these segments can be rolled into pills by a gentle rolling of the two plates on each other, and in this way the machine does not merely cut the cylinder, but also rolls them into pills. Special pill machines are on the market in which the grooved plates are removable from the boards and also from the cutter; and with each machine goes a series of these plates coinciding with the average size of pills. Thus, there is one set of plates for 1-grain pills, 2-grain pills, and 3-grain pills, and one for 5-grain pills. Such machines, however, are rather expensive, and in the average pharmacy the machine is used for cutting rather than for rolling the pills. In purchasing a machine the pharmacist is advised to secure one with plates having at least 36 grooves;the smaller machines, cutting only 12 pills, cost but little less than the wider ones and are not so useful.

Rolling the Pills.—The cut segments, unless rolled in the machines, are taken up between the finger and the thumb and rolled by means of a rotating movement until perfectly spheric. The finishing touches are performed, especially when the mass is hard and difficult to roll between the finger and the thumb, by placing the partially rolled pills on the board of the pill machine, dusting fairly liberally with the dusting powder, covering with a wooden pill roller (Fig. 222), which is then held firmly by the hand and moved over the board, either in the form of circles or in figure eights, the friction between the roller and the board being sufficient to smooth the pills into spheric forms, providing the mass is sufficiently firm. If the pills are soft the pressure exerted must be very gentle, and it is usually advisable, in securing successfully rolled pills, that the depth of the roller be exactly the same as the height of the finished pill. To accomplish this, however, it would be necessary to have a set of rollers of different depths, and this is rarely the case in the average pharmacy.

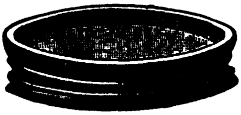


Fig. 222.—Pill roller.

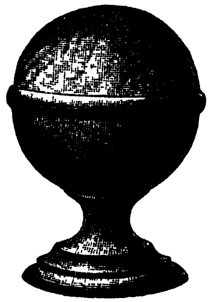


Fig. 223.—Pill silverer.

As mentioned on p. 342, both in rolling and dispensing the pills they are dusted with powder, designed to prevent the pills from sticking together. It is considered good pharmacy to dust the white pills with a white powder, such as a finely powdered starch; while those which are of a dark color are usually dusted with lycopodium powder; glycyrrhiza is used as a dusting powder, especially in Germany, but is not considered as satisfactory as lycopodium. In dispensing ready-made coated pills no dusting powder should be used.

The finished pills are usually dispensed in round boxes, commercially called pill boxes. Of late years square shouldered boxes have come into use among the better pharmacies, and are very satisfactory, although the increased cost over the round pill boxes renders their use less popular than the latter. More recently screw-capped vials are also used. The wrapping of a pill box has already been described on p. 311.

Pills are now made on an enormous scale by machinery, the finest type of which is that made by Arthur Colton, of Detroit. The outfit consists of a kneading machine, which prepares the mass; a rolling machine, in which lumps of the mass are rolled into cylinders; a cutting and finishing machine, which cuts the cylinder into the individual pills and rolls them until spheric or ovoid, as desired. The pills are then dried and coated.

Friable pills are a class introduced by Dr. Upjohn in 1885, and were much vaunted as pills made without excipient and, therefore, capable of disintegrating as soon as the coating is dissolved. The process of manufacturing these pills is exceedingly clever, consisting of placing the mixed powder containing the medicinal substances in a cylindric pill-coating machine (see p. 336), introducing therein a lot of sugar pellets, about 1/4 grain in size and gradually spraying water therein as the coater revolves. As these pellets are rolled in the moistened powder they gradually collect the powder in a way quite similar to making a large snowball by rolling a small one in damp snow. The rotation of the pills is continued until most of the pills are of the desired size. They are then removed from the machine, and are sifted through special colanders with orifices of exactly the size of the pill desired. Thus, in making quinine pills by this method colanders are provided with holes which have been carefully determined as representing 1-grain, 2-grain, 3-grain, and 5-grain pills. Placing the pills of the various sizes into, say, the 3-grain colander, those remaining on the colander weigh over 3 grains, while those falling through are from 1 to 3 grains. By placing those which have fallen through on a 2-grain colander, those smaller than 2 grains pass through, and at last the desired size is obtained. The pills which are smaller than any of the required sizes are returned to the machine, and rotation continued until brought up to the weight desired. The finished pills are rapidly coated with either sugar or gelatin, and are thus dispensed.

C. S. N. Hallberg called attention to the fact that the friable pills presented the same objection as is made to most of the commercial pills—that is, in order to obtain a pill the coating of which will not discolor, the rolled pill is first coated with a layer of plaster of paris and then with the proper coating.

Coating of Pills.—As mentioned above, the fresh pills prepared by the pharmacist are coated merely by dusting with some powder, say, starch or lycopodium. A century ago attempts were made to present the pill in a more attractive appearance by use of special and permanent coating; the first material used for this purpose was French chalk, which is a variety of powdered soap-stone (silicate of magnesium). The coating of pills by this process—called *pearl coating*—consists of placing the finished pill in a small dish containing alcoholic or ethereal solution of balsam of Tolu, thus coating it with enough of the balsam to be thinly varnished. While this varnish is still wet they are thrown into French chalk, the mixture of pills and chalk placed in a small sieve, and an excess of powder removed by sifting. The pills are then placed in a hollow sphere (Fig. 223), the two hemispheres of which were united by means of a screw joint. The pills were rotated in this ball by vigorous agitation, and in this way the excess of chalk was thrown off and that remaining was worked into a smooth, pearly coating. The process of silver or gold coating pills was performed in a manner quite similar, the pills were first varnished, as in the pearl coating, then placed in the hollow globe, containing sheets of gold or silver foil. By rotating the pills the foil adheres to the same, and by vigorous agitation of the globe the coating became uniform and polished.

Balsam of Tolu was directed by former editions of the Pharmacopœia for coating pills of ferrous iodide and pills of phosphorus, the object of the coating being to protect the pill mass from the oxidizing action of the atmosphere. Investigations of Bukey and Bren indicate that pills so coated are frequently insoluble in the fluids of the stomach and intestines.

Sugar coating was first introduced by confectioners for the purpose of coating almonds. Its use in this way was so successful that there soon arose a demand for pills coated in the same manner, and with this demand began the industry of the manufacture of sugar-coated pills.

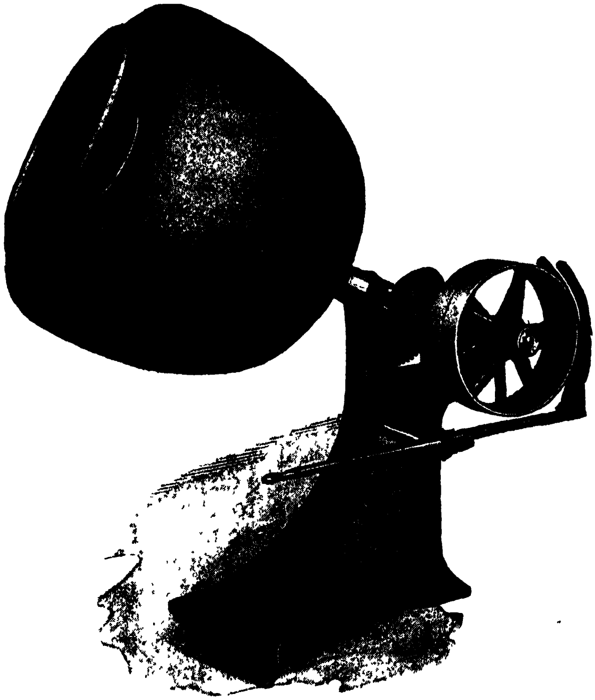


Fig. 224 —Stokes' pill-coating pan.

The process of sugar coating pills is performed in spheric pans (Fig. 224) continuously rotated by means of a central axis operated by electric power. This pan is usually of copper, and is jacketed so that it can be kept uniformly warm with steam. Within the pan a quantity of syrup, almost ready to crystallize, is placed, and when the walls of the pan have become smeared with the syrup, the rounded, dried, uncoated pills are placed therein. As the apparatus rotates, the heat gradually drives off the water from the syrup, with the resulting formation of the layers of sugar on the pills, the process being continued until each pill is uniformly coated with a hard, white, sugary layer. The coated pills are then taken from the apparatus and are rotated in a similar apparatus (Fig. 225) containing paraffin and lined with rough canvas, when the friction, plus the wax, produces a fine polish.

As mentioned above, the great objection to the sugar-coated pills is the fact that, in order that the coating of pills made of dark constituents does not discolor, it is necessary to coat the pill with a layer of plaster of paris, which certainly does not increase the rapid solubility of the pill. Of late, manufacturers have been placing on the market chocolate and pink-coated pills. These are prepared in a manner similar to the white-coated pills, with the exception that in the first case a small amount of chocolate is added to the syrup, while in the case of pink, carmine coloring is added to the syrup.

Many of the so-called "chocolate-coated" pills are really covered with burnt umber and other forms of ferric oxide. They are labeled "brown coated" rather than "chocolate coated" to comply with the Food and Drug law.

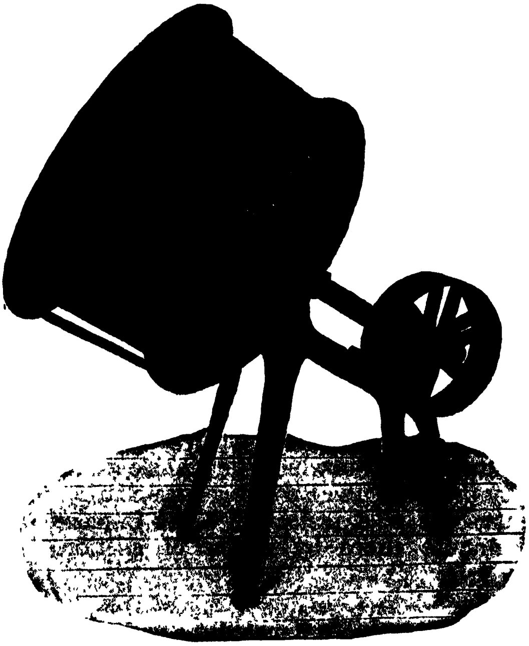


Fig. 225.—Stokes' pill polisher.

The sugar coating of pills is a process which cannot be done by the retail pharmacist, the coating pan requiring steam power and steam heat. Several schemes of hand-made sugar-coated pills have been suggested, but when tried by the writer, have never yielded satisfactory results. As the public is now demanding sugar- and gelatin-coated pills, the art of pill-making is rapidly falling into disuse.

Gelatin coating of pills is usually made by large manufacturers but the art is not beyond the reach of the retail pharmacist, as several varieties of gelatin-coating apparatus are now on the market at moderate prices. Essentially, the process consists of impaling each pill on a long needle and dipping the same into a solution of gelatin of the proper consistence. A satisfactory gelatin solution is made as follows: gelatin 200; macerate with cold water, 200; then add hot water, 640; mucilage, 200 (acacia, 100; water, 300); syrup, 400; glycerin, 60. Dissolve by gentle heat and then strain. More expensive coating apparatus merely perform the coating with greater expedition, the needles being arranged in groups, which make it convenient to handle considerable quantities of pills at one time, and which also make the coated pills dry easier.

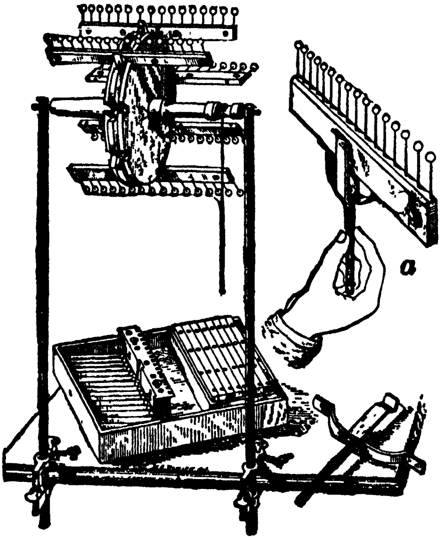


Fig. 226.—Patch's gelatin pill-coater.

Two typical coating machines for the retail pharmacist are the Patch machine and the Maynard machine. In the Patch machine the pills are impaled on the teeth of a comb (*a*); the ingenious part of the process is the drying apparatus, which consists of a wheel holding seven such combs, rotating by means of a string (Fig. 226). In the Maynard machine the needles are grouped on a circular disk, corresponding to the depressions in a circular plate which holds the pills while being impaled. The impaled pills are then dipped into the gelatin solution and are dried by rapidly whirling the disk holding them. When the coating is dry, the pills are loosened from the pins by pressing down a special plate in the twirler (Fig. 227).

The manufacture of pills by this process yields an admirable gelatin coating, which, however, has been criticized by reason of the fact that they contain minute orifices—the pinholes. The presence of this pinhole can in no way interfere with the finished pill, and, if anything, will aid in solubility. But this so-called "defect" has been seized as an opportunity of manufacturing a pill in which the pinhole would be avoided. This is accomplished by means of the Russell gelatin-coating machine. In this ingenious apparatus the pills, instead of being impaled on pins, are held on the end of minute tubes by means of suction. The apparatus consists of a hollow steel plate, the flat sides of which are provided with a series of minute tubes. Suction is applied by means of flexible tubing connecting the plate with an air pump, when the plate is held over a disk containing hemispheric depressions exactly corresponding in number and position to the tubes in the plate. In each depression is mechanically rolled a pill, and the moment the plate is placed over the pills, they are

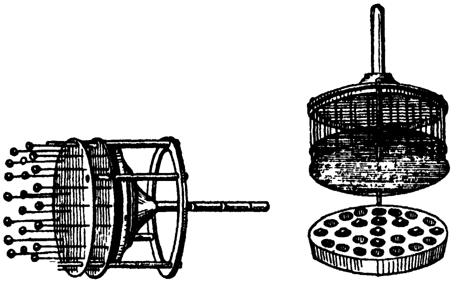


Fig. 227.—Maynard's gelatin coater.

sucked to the ends of the tubes and are thus firmly held. The pill is then dipped into the gelatin solution, coated half way, turned upward, and allowed to dry, the stop-cock at the end of the plate being closed, thus continuing the vacuum in the plate even after the rubber tube connected with the air pump has been removed. The tubing is then connected with another plate of the same kind, and another set of pills are coated; and in this way the coating is continued until a number of such plates have been filled with the pills and half coated. The plates containing half-coated pills have, in the meanwhile, been placed on a special apparatus (Fig. 228) consisting of an endless chain carrier, and have been gradually moving toward the other end of the frame, where they are taken charge of by the second operator, who transfers the pills to a second plate by suction in such a way that they are grasped by their coated ends, which are now dry. The pills are then dipped again into the gelatin solution, and the second half of the coating thus completed. The pills are then placed once more on the endless chain carrier, and by the time they reach the other end of the frame they are thoroughly coated and perfectly dry.

Enteric pills are a special form of pill which are intended to pass through the acid juices of the stomach without dissolving, to dissolve in the alkaline juices of the small intestine. To accomplish this result it is necessary to coat such pills with a material which dissolves in alkalis and not in acids, and for this purpose salol is employed, the pills being rolled five times in melted chemical. Toplis uses as an enteric coating stearic acid dissolved in ether, the manipulation resembling coating pills of phosphorus, as described on page 343.

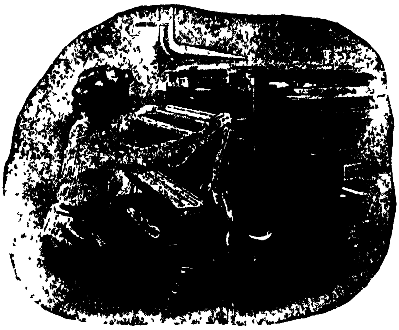


Fig. 228—Russell's gelatin coater.

Freeman coats capsules with stearic acid by dipping same into the fused chemical. Wruble recommends as enteric coating an ammoniacal solution of shellac; that is a saturated solution of shellac in 10 per cent ammonia water.

Gelatin capsules may be made useful for enteric purposes by dipping in formaldehyde solution. Scoville however points out that the method is useful only in special cases. Volweiler has patented a process for coating capsules with a cellulose ester dissolved in a suitable solvent.

The substance originally employed for coating enteric pills was keratin, a commercial product prepared from goose quills. Puckner has shown however that practically all commercial keratins dissolve in the stomach: hence are useless for enteric pill coating. Salol has been recommended as an enteric coating. It liquefies when heated and the pills are rotated in the liquefied salol while it is cooling and solidifying.

Before proceeding to a consideration of the official pills, attention should be called to the admirable monograph on pills found in the present edition of the National Formulary and particularly to the manipulations of various coatings, notably Tolu coating.

TABLE OF OFFICIAL PILLS

Process	*Excipient*	*Galenic preparations*	*Chemical preparations*
Massing and rolling. Uncoated.	Diluted alcohol.	Compound pills of colocynth and jalap (N.F. VI). Compound pills of mild mercurous chloride (N. F. VI).	
	Glucose.	Pills of aloe and myrrh (N.F. VI). Pills of aloin, strychnine and belladonna (N.F. VI). Pills of aloin, strychnine, belladonna and cascara (N.F. VI). Pills of aloin, strychnine, belladonna and ipecac (N.F. VI). Compound pills of cascara (N.F. VI). Pills of iron, quinine, strychnine and arsenic (N.F. VI).	
	Glucose and water.	Compound pills of rhubarb (N.F. VI).	
	Glycerin and water.	Pills of aloe and mastic (N.F. VI).	
	Soap and water.	Pills of aloe. Pills of asafetida (N.F. VI).	
	Tragacanth, glycerin and water.		Pills of ferrous carbonate.
Coated pills.	Acacia and water.		Pills of ferrous iodide (N.F. VI).

SPECIAL NOTES ON OFFICIAL PILLS

PILULÆ ALOES—Pills of Aloe

(Pil. Aloe)

Condensed Recipe.

Ingredients.—Aloe, 13 Gm.; powdered hard soap, 13 Gm.; water, enough.

Manipulation.—Triturate the powders, mass with water and divide into 100 pills.

Dose.—Two pills.

PILULÆ FERRI CARBONATIS—Pills of Ferrous Carbonate

These pills, commonly called *Blaud's pills,* depending for their activity upon a chemical action, can best be discussed among the iron preparations in Part III.

Pilulæ Asafœtidæ (U.S.P. X; N.F. VI) or *Pills of Asafetida* are made from asafetida, 20 Gm.; powdered hard soap, 6 Gm.; water, enough to mass the solids and divide into 100 pills. They are directed to be coated, preferably with gelatin. When a suitable coating is not at hand the pill mass may be dispensed in gelatin capsules. *Dose.*—Two pills.

Pilulæ Hydrargyri Chloridi Mitis Compositæ (U.S.P. X; N.F. VI) or *Compound Pills of Mild Mercurous Chloride,* also more commonly known as compound cathartic pills or *C.C. pills* contain compound extract of colocynth, mild mercurous chloride (calomel), resin of jalap, and gamboge, made into a mass with diluted alcohol. After years of great popularity under the name of *compound cathartic pills*, these pills come under the ban of the medical extremists who, under the argument that therapeutically suggestive names are objectionable, buried these unfortunate pills under the formidable name of five words given above in the U.S.P. X and omitted them entirely from the U.S.P. XI. They are however still listed in the National Formulary. Throughout this book the old name "compound cathartic pills" will still be used whenever these pills are mentioned. *Dose.*—Two pills.

Pilulæ Phosphori (U.S.P. X) or *Pills of Phosphorus* are made to contain about $\frac{1}{100}$ grain of phosphorus in each pill. They are prepared by mixing a chloroformic solution of phosphorus with althea and acacia, adding the excipient, glycerin and water, and rapidly massing, cutting, and rolling into pills. The massing must be done rapidly, as phosphorus long exposed to air takes fire spontaneously. The ignition is due to the oxidation of phosphorus, and to prevent this oxidation in the finished pills the Pharmacopœia directed that they be coated with balsam of Tolu. *Dose.*—One pill.

Pilulæ Ferri Iodidi (U.S.P. IX; N.F. VI) *Blancard's Pills* or *Pills of Ferrous Iodide*, are prepared by utilization of a chemical reaction; hence they will be discussed among the iron preparations on page 564.

Pilulæ Rhei Compositæ (U.S.P. IX; N.F. VI) contain rhubarb, aloe, myrrh and oil of peppermint. Glucose and water are used as excipient. *Dose.*—Two pills.

PILLS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients. (figures show amount used in each pill)	Excipient.	Remarks.
Pilulæ aloes et mastiches.	Pills of aloe and mastic (U.S.P. VIII).	Aloe 0.13 Gm., mastic 0.04 Gm.; red rose.	Glycerin and water.	The well-known *Lady Webster's after dinner pill.* *Dose.*—2 pills.
Pilulæ aloes et myrrhæ.	Pills of aloe and myrrh (U.S.P. VIII).	Aloe 0.13 Gm.; myrrh, 0.06 Gm.; aromatic powder.	Glucose.	*Dose.*—2 pills.
Pilulae aloini, strychninæ, belladonnæ et cascaræ.	Pills of aloin, strychnine, belladonna and cascara.	Aloin, 0.013 Gm.; strychnine, 0.0005 Gm.; extract of belladonna, 0.008 Gm.; extract of cascara sagrada, 0.0325 Gm.; glycyrrhiza.	Glucose.	*Dose.*—1 pill.
Pilulae aloini, strychninæ, belladonnæ et ipecacuanhæ.	Pills of aloin, strychnine, belladonna and ipecac.	Aloin, 0.016 Gm.; strychnine, 0.001 Gm.; extract of belladonna, 0.008 Gm.; ipecac, 0.004 Gm.; glycyrrhiza.	Glucose.	*Dose.*—1 pill.
Pilulae aloini, strychninæ et belladonnæ.	Pills of aloin, strychnine and belladonna.	Aloin, 0.013 Gm.; strychnine, 0.001 Gm.; extract of belladonna, 0.008 Gm.	Glucose.	The well-known "*A.S.* and *B. pill.*" *Dose.*—1 pill.
Pilulæ asafœtidæ	Pills of asafetida.	Asafetida, 0.2 Gm.	Soap and water.	*Dose.*—2 pills.
Pilulæ cascaræ compositæ.	Hinkle's pills.	Extracts of belladonna and cascara sagrada; aloin; resin of podophyllum; strychnine sulfate; oleoresin of ginger; glycyrrhiza.	Glucose.	*Dose.*—1 pill.
Pilulæ colocynthidis et jalapæ compositæ.	Vegetable cathartic pills, (N.F. V).	Compound extract of colocynth, 0.06 Gm.; extracts of hyoscyamus and leptandra; resins of jalap and podophyllum; oil of peppermint.	Diluted alcohol.	*Dose.*—1 pill.
Pilulæ ferri iodidi.	....	....	....	See above.
Pilulæ ferri, quininæ, strychninæ et arseni.	Aitkin tonic pill.	Reduced iron; quinine sulfate; strychnine and arsenic trioxide, of each, 0.0013 Gm.	Glucose.	*Dose.*—1 pill.
Pilulæ hydrargyri chloridi mitis compositæ.	Compound cathartic pills, U.S.P. X.	Compound extract of colocynth, 0.08 Gm.; mild mercurous chloride, 0.06 Gm.; resin of jalap, 0.02 Gm.; gamboge, 0.015 Gm.	Diluted alcohol.	*Dose.*—2 pills.
Pilulæ rhei compositæ.	....	....	....	See above.

DOSES OF OFFICIAL PILLS

1 pill: Pills of aloin, strychnine and belladonna (N.F. VI); aloin, strychnine, belladonna and cascara (N.F. VI); aloin, strychnine, belladonna and ipecac (N.F. VI); cascara compound (N.F. VI); colocynth and jalap compound (N.F. VI), and iron, quinine, strychnine and arsenic (N.F. VI).

2 pills: Pills of aloe; aloe and mastic (N.F. VI); Aloe and myrrh (N.F. VI); asafetida (N.F. VI); ferrous iodide (N.F. VI); mild mercurous chloride compound (N.F. VI); and rhubarb compound (N.F. VI).

3 pills: Pills of ferrous carbonate.

LABORATORY EXERCISES

MAKE PILLS OF ACETANILID

Powdered acetanilid	1 Gm.

Put on pill tile, and bring in contact with a spatula containing a sufficient amount of excipient. Knead the excipient into the powder by means of the spatula until a pliable pill mass is obtained. Scrape the mass into one lump, dust the pill tile with powdered starch, roll the pill mass out with the spatula into a cylinder like a pencil until it is the length of ten divisions on the scale on the tile. Then cut the cylinder with spatula into 10 equal parts, and roll each between *clean* thumb and forefinger until perfectly spheric. Then put in pill box, dust with starch, wrap box in paper, making a neat package (p. 311).

Remarks.—*Excipient.*—Substance used to make drugs, liquids as well as solids, into plastic mass (p. 332).

A good excipient for powders is glycerite of tragacanth:

Powdered tragacanth	3 drachms
Triturate with glycerin	3 fluidrachms
Then add water	½ fluidounce

Transfer jelly into appropriate jars.

The *amount of excipient required* can be learned only by experience. Roughly speaking, in above case a lump about the size of a pea should suffice. To make a good mass the entire amount of excipient required should be added at one time.

If mass is too soft, add another 1 Gm. powdered acetanilid and make 20 pills.

Masses are made on tiles only when small amounts of pills are to be made, and when there is no difficulty in forming the mass.

Pliable Pill Mass.—See p. 334.

Cutting pills on tile with spatula gives irregular results. Every drug store should have a pill cutter. (See p. 333.)

Pills are dusted to prevent their sticking together. White pills should be dusted with powdered starch; dark pills, with lycopodium.

MAKE COMPOUND CATHARTIC PILLS

Recipe.—Compound extract of colocynth	2.00 Gm.
Mild mercurous chloride	1.50 Gm.
Resin of jalap, in fine powder	0.50 Gm.
Gamboge, in fine powder	0.37 Gm.
Diluted alcohol, a sufficient quantity.	
To make	25 pills

Mix the powders intimately, then incorporate a sufficient quantity of diluted alcohol to form a mass, and divide it into 25 pills.

Remark on Process.—The recipe just given is similar to but not identical with that given in the present edition of the Formulary in which, however, the official name of these popular pills has been changed to "Compound Pills of Mild Mercurous Chloride." The two recipes should be carefully compared by the student.

In *triturating powders* always first rub up the ingredients prescribed in smallest amount with a small quantity of the other substances, and add the rest of the drugs gradually with constant stirring—this to insure thorough blending of the most potent drugs.

The *excipient* in this case is diluted alcohol, with which the compound extract of colocynth will combine to make a plastic mass. Five drops should suffice, provided enough "elbow grease" is used. In fact, if the mortar is warmed and the pestle is handled vigorously, the mass can be formed without use of diluted alcohol.

Working up the mass in a mortar with a pestle is a process hard to explain in words. The pestle is firmly grasped in the right hand with the end of the handle resting against the center of the palm, while the mortar is held fast with the left hand. The mass is worked by pressing down on it with the pestle with a rotary movement to the right. From time to time the mass is carefully scraped from the pestle and from the sides of the mortar and worked again, the process being continued until a thoroughly plastic mass results.

Cutting the cylinder into pills must be done indirectly when the scale on the pill tile is for 10 or 20 pills, if 25 pills are directed. If the scale has 20 markings, roll the cylinder out to 20 and cut into 5 equal lengths (4 spaces each). Then take each length and roll until it is 5 spaces long, and cut into 5 pills. Treating the other lengths similarly, we have in the end 25 pills. It is needless to say that great care should be taken to have the cylinder of exactly the same thickness through its entire length. In practice a pill cutter (p. 333) should be used.

Roll pills between the first finger and thumb as in making pills of acetanilid.

Dust pills with lycopodium.

MAKE PILLS OF PHOSPHORUS

Recipe.—	Phosphorus	0.015 Gm.
	Althea, in No. 60 powder	1.500 Gm.
	Acacia, in fine powder	0.750 Gm.
	Chloroform,	
	Glycerin,	
	Water,	
	Balsam of Tolu,	
	Ether, each, a sufficient quantity,	
	To make	25 pills

Dissolve the phosphorus, in a test tube, in about 2 cc. of chloroform, with the aid of a very gentle heat, replacing from time to time any of the chloroform which may be lost by evaporation. Mix the althea and acacia in a mortar, next add the solution of phosphorus, then immediately afterward a sufficient quantity (about 1 cc.) of a mixture of 2 volumes of glycerin and 1 volume of water, and quickly form a mass; divide it into 25 pills.

Dissolve 10 Gm. balsam of Tolu in 15 cc. of ether, shake the pills with a sufficient quantity of this solution until they are uniformly coated, and put them on a plate to dry, occasionally rolling them about until the drying is completed.

Keep the pills in a well-stoppered bottle.

Remarks on Process.—The recipe just given is similar to but not identical with that given in the previous edition of the Pharmacopœia. The two recipes should be carefully compared by the student.

Handling the phosphorus must be done with care, as it is very unstable, igniting spontaneously when exposed too long to the air. Phosphorus should always be weighed *under water*, that is, a beaker or other vessel containing water should be counterpoised on the scale, and the phosphorus immersed in water while weighing. In the same way the large piece of phosphorus should be cut while under water contained in pint evaporating dish.

The *cutting of phosphorus* is easy, since it is a soft, waxy solid, readily sliced with an ordinary knife. Always cut off the outer oxidized layer, and use the fresh phosphorus from the middle of the stick.

The *solution of phosphorus* is made by quickly freeing the weighed phosphorus from adhering water by pressing between filter paper and dropping the lump into the chloroform contained in a test tube before the phosphorus has time to ignite. If the phosphorus dissolves slowly in the chloroform, the solution can be aided by the use of gentle heat, adding extra chloroform to make up for loss of evaporation.

The *mass must be worked up* as rapidly as possible lest it *catch fire*. If it does ignite, carry to sink and turn on the water from the faucet.

Use enough excipient to make a rather soft mass, for a firm mass becomes rubber-like on rolling out. Ten to 12 drops usually suffice.

In cutting the pill cylinder use the same plan as with compound cathartic pills if the pill tile scale has not 25 spaces. Use lycopodium as a dusting powder.

Coating the pills does not yield handsome results; in fact, no pill coating can be well done without special appliances. (See p. 335.) In this special case the coating is not put on to enhance the appearance of the pill, but to protect it from atmospheric action (p. 335). In coating, put pills in small dish, pour on 10 to 20 drops of the tolu solution, and rotate until dry. Then, if necessary, add more tolu solution and rotate further.

DOSES OF OFFICIAL PILLS

As already mentioned, pills, troches, and suppositories differ from other classes of official pharmaceuticals taken internally in the fact that the finished products are subdivided into definite doses; hence while the dosage of other preparations are by weight or volume, we administer pills and troches by a certain number of subdivided particles.

COMPRESSED TABLETS

These are lenticular masses of medicinal substances forced into a solid mass by compression. Compressed tablets were introduced by Brockedon in 1843, and soon became popular by reason of their convenience and simplicity of manufacture. It must be said, however, that compressed tablets are open to the possible objection of insolubility. Many substances, when compressed sufficiently firmly to hold together, are very difficultly soluble. In the manufacture of compressed tablets this should be borne in mind, and care should be exercised in so blending the ingredients as to render them as soluble as possible under the circumstances.

The making of such compressed tablets depends chiefly on the proper blending of the ingredients, foreign substances being added either to secure solubility or to prevent sticking in the mold. These added inert constituents can be roughly grouped under the word excipient. For each combination of chemicals the excipient should be studied, even as we do in the case of pills, and the special directions are beyond the limits of this work. Suffice it here to cite a typical combination for a mass intended for compression. For this purpose a medicinal substance is combined with one tenth its weight of sugar and one twentieth its weight of gum arabic. The mass is then mixed with a little water, granulated by passing through a coarse sieve, and then carefully dried. The dried granular mass is then sprayed with liquid petrolatum, 10 or 12 drops being enough for a pound of mass. Such mass, on compression, yields a tablet that is fairly soluble, while the lubricant (liquid petrolatum) is squeezed out upon the surface of the compressed tablet, thus preventing the mass from sticking to the mold.

For the purpose of preventing the mass from adhering to the dies of the machine, talcum is sometimes used; the talcum preventing the "picking" or adhesion of minute portion of the surface of the tablet from sticking to the die; while liquid petrolatum prevents nicking of the edges. Talcum if used at all should be employed very sparingly and liquid petrolatum is never used in tablets intended to be water-soluble.

Fantus and Snow find that the sticking of the tablet to the die is largely obviated by adding to the tablet mass 20 per cent of "Fat Starch," which consists of 25 parts of liquid petrolatum triturated with 75 parts of starch.

Rapp finds that pectin is a valuable addition to the tablet excipient, whereas Thomann finds pectin and dextrin objectionable. Thoenessen recommends the mucilage of quince seed or of agar as excipients.

In modern large-scale tablet making the adhesive excipients are gelatin or acacia. These are never added (as formerly) as dry powders but as jellies or solutions; since the dry adhesive produces difficultly soluble tablets. Using moist adhesives produces a soft mass that has to be dried in special dryers before it is in shape for granulation. When sufficiently dry for granulation the mass is forced through a No. 20 sieve and after further drying the granules are shaken on a No. 30 sieve, since successful compression demands granules of not more than 20 nor less than 30 mesh.

A modern tablet to be successful must disintegrate quickly when thrown into water. The best method of making a quickly disintegrating tablet is to add to the tablet mass potato starch (1/16 to 1/8 grain per tablet). Magnesium peroxide is also used for the same purpose.

In making tablets for water-soluble chemicals, no excipient is necessary; the granulated chemical being fed directly into the tablet machine.

In making compressed tablets of quinine it is essential that the quinine be in a satisfactory condition before attempting to compress it, as otherwise they are almost sure to adhere to the mold. The quinine should be at first sufficiently dried, and then should be granulated and sprayed with liquid petrolatum.

The apparatus used in compressing tablets consists, in its simplest form, of a steel cylinder pierced with a central bore, in which fits a plunger the end of which is convex, while at the other end of the cylinder fits the lower die, consisting of a cylindric piece of steel similar to the plunger, but shorter, terminating in a broad base. The cylinder is fitted to the lower die and the quantity of powder directed to be compressed is placed within the bore (Fig. 229). The plunger is then inserted, and the mass is then pressed against the lower die, forming a firm lenticular disk if the pressure be sufficient. The pressure is produced either by hitting the plunger with a hammer or mallet or by means of an iron lever. This lever is sometimes in the form of a long handle acting from a hinge. Of these machines, the one in which compression is performed with a hammer has fallen into disuse, on account of the noise accompanying the process and its general unsatisfactory character. The lever machine is simple and inexpensive, and should be found in every pharmacy for the manufacture of extemporaneous tablets. An excellent modification of the lever compressor is shown in Fig. 230. A very good investment for the prescription department is the more expensive machine, as shown

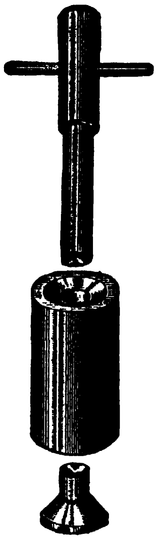
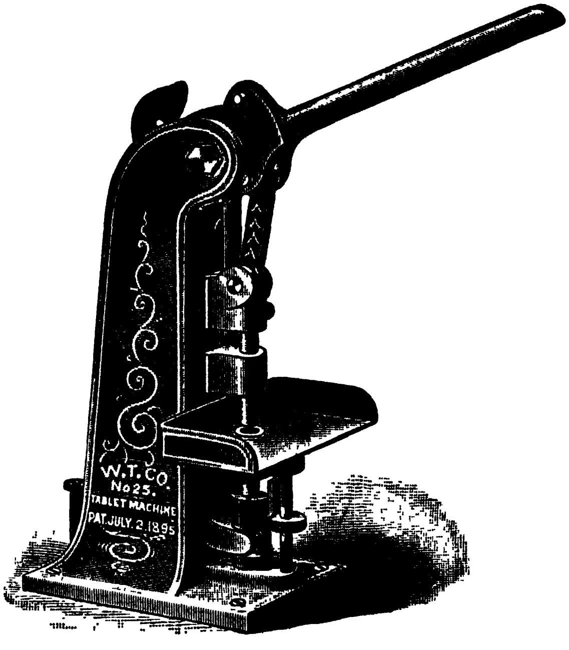


Fig. 229 —Compressed tablet mold.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No 25.
TABLET MACHINE
PAT. JULY. 2. 1895

Fig. 230.—Compressed tablet machine.

in Fig. 231. In these machines the tablet mass is blended, then placed in the appropriate funnel, and the mechanism is worked by a crank on the end of the circular wheel which transmits power not merely to cause the automatic rise and fall of the two dies, thus pressing the tablets, but also to cause the throwing out of the funnel the quantity of the mass required for each tablet, and the flipping aside of the finished tablet. Such a tablet machine, known as the Stokes' "Eureka" machine, will readily make 100 tablets a minute. In large manufacturing concerns tablet machines having a higher efficiency are used, most notable of these being the Stokes-Clark rotary tablet machine (Fig. 232). In this machine there is a series of dies (12 to 25) operating on a circular plate, and being mechanically raised and lowered during the revolution of the plate by means of cams; each revolution of the plate, therefore, produces 12 to 25 tablets, and as the machine can be run very rapidly, it is capable of turning out from 30,000 to 50,000 tablets an hour.

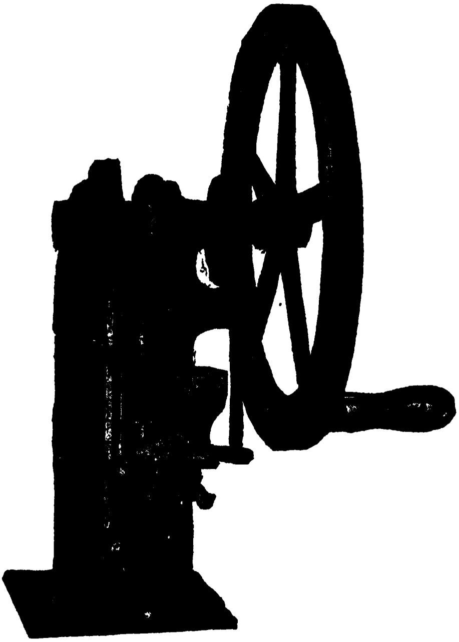


Fig. 231.—Stokes' "Eureka" tablet machine.

The present Pharmacopœia recognizes 3 compressed tablets, the large and small mercury bichloride tablets and tablets of nitroglycerin. The National Formulary recognizes forty-eight compressed tablets and provides upper and lower limits or tolerances. (See pages 348 and 349.)

TABELLÆ GLYCERYLIS TRINITRATIS—Tablets of Glyceryl Trinitrate

(Tab. Glyceryl. Trinitrat.—Tablets of Nitroglycerin, Trinitrin Tablets)

Tablets of Glyceryl Trinitrate contain not less than 87.5 per cent and not more than 112.5 per cent of the labeled amount of $C_3H_5(NO_3)_3$, including all tolerances.

Assay.—See U.S.P., p. 379 and for other details regarding nitroglycerin see page 679 of this book.

Dose.—An amount corresponding to 0.0006 Gm. (1⁄100 grain).

TOXITABELLÆ HYDRARGYRI BICHLORIDI MAGNÆ—Large Poison Tablets of Mercury Bichloride

(**Toxitabel. Hydrarg. Bichlor. Mag.**—Toxitabellæ Hydrargyri Chloridi Corrosivi U.S.P. X, Large Corrosive Sublimate Tablets, Large Bichloride Tablets)

Large Poison Tablets of Mercury Bichloride contain an average of not less than 0.45 Gm. and not more than 0.55 Gm. of $HgCl_2$, with a sufficient quantity of a suitable excipient or diluent.

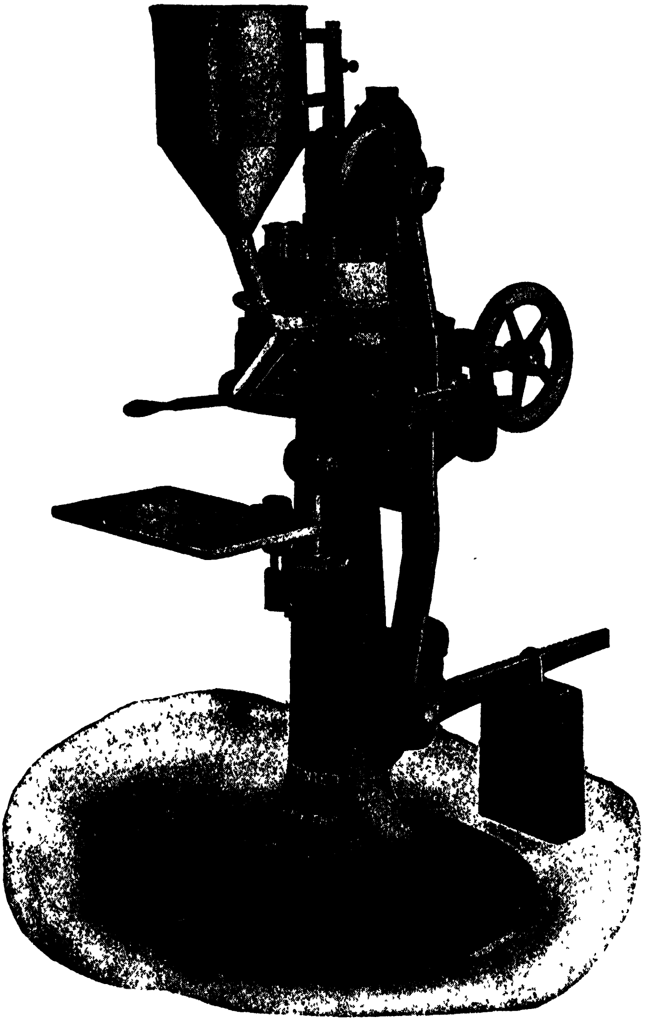


Fig. 232.—Stokes-Clark rotary tablet machine.

These tablets must be of a distinctive color, not white; they must be of an angular or irregular shape, not discoid. When sold in small quantities suitable for household use, they must be dispensed in glass containers of a distinctive, angular shape having irregular or roughened sides or edges. On the exterior of each container must be placed a red printed label bearing the word "POISON" and a statement indicating the amount of mercury bichloride in each tablet. (See "Remarks" on page 349.)

TABLETS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Prescribed limits of labeled amount of active ingredient including all tolerances.
Tabellæ acetanilidi.	Tablets of acetanilid.	92.5% to 107.5%.
Tabellæ acetophenetidini.	Phenacetin tablets.	92.5% to 107.5%.
Tabellæ acetophenetidini et phenylis salicylatis.	Phenacetin and salol tablets.	90% to 110%.
Tabellæ acidi acetylsalicylici.	Aspirin tablets.	92.5% to 107.5%.
Tabellæ aminopyrinæ.	Amidopyrine tablets.	92.5% to 107.5%.
Tabellæ ammonii chloridi.	Tablets of ammonium chloride.	94% to 106% for tablets of 0.3 Gm. or more; 92.5% to 107.5% for tablets of less than 0.3 Gm.
Tabellæ apomorphinæ hydrochloridi.	Tablets of apomorphine hydrochloride.	91% to 109%.
Tabellæ arseni trioxidi.	Arsenous acid tablets.	92.5% to 107.5%.
Tabellæ atropinæ sulfatis.	Tablets of atropine sulfate.	92.5% to 107.5% for tablets of 0.02 Gm. or more; 91% to 109% for tablets of less than 0.02 Gm. but not less than 0.0012 Gm.; 88% to 112% for tablets of less than 0.0012 Gm.
Tabellæ barbitali.	Tablets of barbital.	92.5% to 107.5% for tablets of more than 0.07 Gm.; 91% to 109% for tablets of 0.07 Gm. or less.
Tabellæ barbitali solubilis.	Tablets of barbital sodium.	
Tabellæ bismuthi subcarbonatis.	Tablets of bismuth subcarbonate.	83% to 97%
Tabellæ bismuthi subgallatis.	Tablets of bismuth subgallate.	48% to 61%
Tabellæ bismuthi subnitratis.	Tablets of bismuth subnitrate.	73% to 85%.
Tabellæ bromidorum trium.	Triple bromide tablets.	70% to 81% bromine.
Tabellæ caffeinæ citratæ.	Tablets of citrated caffeine.	43% to 53%.
Tabellæ caffeinæ cum sodii benzoate.	Tablets of caffeine with sodium benzoate.	43.5% to 53.5%.
Tabellæ calcii carbonatis.	Tablets of calcium carbonate.	92.5% to 107.5%.
Tabellæ calcii lactatis.	Tablets of calcium lactate.	92.5% to 107.5%.
Tabellæ cinchopheni.	Tablets of cinchophen.	92.5% to 107.5%.
Tabellæ cocainæ hydrochloridi.	Tablets of cocaine hydrochloride.	91% to 109%.
Tabellæ codeinæ phosphatis.	Tablets of codeine phosphate.	63% to 77%.
Tabellæ codeinæ sulfatis.	Tablets of codeine sulfate.	91% to 109%.
Tabellæ ephedrinæ hydrochloridi.	Tablets of ephedrine hydrochloride.	91% to 109%.
Tabellæ hydrargyri chloridi mitis.	Calomel tablets.	92.5% to 107.5%.
Tabellæ hydrargyri chloridi mitis et sodii bicarbonatis.	Calomel and soda tablets.	92.5% to 107.5% for tablets of more than 0.015 Gm.; 90% to 110% for tablets of 0.015 Gm. or less.
Tabellæ hydrargyri iodidi flavi.	Tablets of yellow mercurous iodide.	91% to 109%.
Tabellæ hydrargyri iodidi rubri.	Tablets of red mercuric iodide.	91% to 109%.
Tabellæ methenaminæ.	Tablets of methenamine.	94% to 106%.
Tabellæ methenaminæ et sodii biphosphatis.	Tablets of methenamine and acid sodium phosphate.	92.5% to 107.5% methenamine.
Tabellæ morphinæ et atropinæ sulfatum.	Tablets of morphine and atropine sulfates.	91% to 109%.
Tabellæ morphinæ sulfatis.	Tablets of morphine sulfate.	92.5% to 107.5%.

Latin name.	English name or synonym.	Prescribed limits of labeled amount of active ingredient including all tolerances.
Tabellæ phenobarbitali.	Tablets of phenobarbital.	92.5% to 107.5% for tablets of more than 0.07 Gm.; 91% to 109% for tablets of 0.07 Gm. or less.
Tabellæ phenobarbitali solubilis.	Tablets of soluble phenobarbital.	
Tabellæ phenolphthaleini.	Tablets of phenolphthalein.	92.5% to 107.5%.
Tabellæ phenylis salicylatis.	Salol tablets.	91% to 109%.
Tabellæ potassii chloratis.	Tablets of potassium chlorate.	94% to 106%.
Tabellæ potassii iodidi.	Tablets of potassium iodide.	94% to 106% for tablets of 0.3 Gm. or more; 92.5% to 107.5% for tablets of less than 0.3 Gm.
Tabellæ potassii permanganatis.	Tablets of potassium permanganate.	
Tabellæ procainæ hydrochloridi.	Tablets of procaine hydrochloride.	92.5% to 107.5%.
Tabellæ quininæ sulfatis.	Tablets of quinine sulfate.	91% to 109%.
Tabellæ scopolaminæ hydrobromidi.	Hyoscine hydrobromide tablets.	91% to 109% for tablets of 0.0012 Gm.; 88% to 112% for tablets of less than 0.0012 Gm.
Tabellæ sodii bicarbonatis.	Tablets of sodium bicarbonate.	92.5% to 107.5%.
Tabellæ sodii bromidi.	Tablets of sodium bromide	92.5% to 107.5%.
Tabellæ sodii nitritis.	Tablets of sodium nitrite	91% to 109%.
Tabellæ sodii salicylatis.	Tablets of sodium salicylate.	91% to 109%.
Tabellæ strychninæ nitratis.	Tablets of strychnine nitrate.	92.5% to 107.5% for tablets of 0 02 Gm. or more; 91% to 109% for tablets of less than 0.02 Gm , but not less than 0 0012 Gm ; 88% to 112% for tablets of less than 0 0012 Gm.
Tabellæ strychninæ sulfatis.	Tablets of strychnine sulfate.	

Remarks.—This and the small "poison tablet" (Bernays) were made official in response to a demand that the use of antiseptic tablets containing mercuric chloride be safeguarded by making them of distinctive shape and color. The outlines of the official monographs given on page 347 and below are self-explanatory.

TOXITABELLÆ HYDRARGYRI BICHLORIDI PARVÆ—Small Poison Tablets of Mercury Bichloride

(Toxitabel. Hydrarg. Bichlor. Par.—Small Corrosive Sublimate Tablets, Small Bichloride Tablets)

Small Poison Tablets of Mercury Bichloride contain an average of not less than 0.1125 Gm. and not more than 0.1375 Gm. of $HgCl_2$, with a sufficient quantity of a suitable excipient or diluent.

These tablets must be of a distinctive color, not white; they must be of an angular or irregular shape, not discoid. When sold in small quantities suitable for household use, they must be dispensed in glass containers of a distinctive, angular shape having irregular or roughened sides or edges. On the exterior of each container must be placed a red printed label bearing the word "POISON" and a statement indicating the amount of mercury bichloride in each tablet.

Assay.—See U.S.P., p. 411.

Phillips suggests that antiseptic "poison tablets" be coated with a wax consisting of equal parts of candelilla wax and a paraffin melting at 56° C. Tablets thus coated will pass through the alimentary tract, undissolved and unchanged. When used, the tablet is broken and its contents will readily dissolve.

Tabellæ (N.F.).—Under this title the National Formulary V gave a monograph describing tablet making, discussing both compressed tablets and tablet triturates. In addition to the general monograph the N.F. V also recognized 7 compressed tablets. The N.F. VI excludes the monograph but gives standards for 48 different tablets.

Individual monographs include upper and lower tolerance limits but do not prescribe a tablet of any given strength, thus making the standards applicable to tablets of any given dosage. The average dose of the drug is given in each monograph. Tests for identity, and in some cases purity, as well as an assay are given in each case.

TABLET TRITURATES

These are flat disks containing medicinal substances, prepared by making a paste of the substance and forcing it into the orifices of a special tablet machine. This machine, as will be seen in Fig. 233, consists of a plate of steel or gutta-percha pierced with a number of accurately bored holes, all of which are of the same size.

The second part of the apparatus consists of a plate, which is studded with cylinders exactly fitting in the orifices of the perforated plate, and of sufficient length to project from 1/8 to 1/16 inch above the perforated plate when it is fitted on these cylinders. The drug is usually mixed with sugar of milk which acts as the base or filler.

In using such a tablet triturate machine, the mass, as above stated, is made into a thin paste by treatment with 75 per cent alcohol, and is forced into the orifices of the perforated plate (which rests on a pill tile or glass plate) by rubbing with a spatula, and the mass is left in holes until firm. The plate is then placed over the studded plate and gradually pressed down over the projecting posts. As these posts pass into the orifices of the perforated plate the dry disks of medicinal substances rise upon the posts and finally emerge from the plate in which they were formed, and they are allowed to remain on the top of the posts until perfectly dried, when a gentle tilting of the apparatus, or the tapping of it with a spatula, will cause them to fall off.

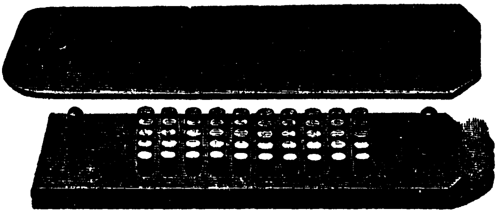


Fig. 233.—Tablet triturate mold.

Tablet triturates were introduced in order to make preparations similar to compressed tablets, but more soluble by reason of their lesser compression.

The disadvantage of these tablet triturates lies in the fact that when they become dry they are liable to disintegrate, and care must be taken in dispensing such in a pill box to provide a sufficient amount of cotton to prevent their shaking to and fro.

HYPODERMIC TABLETS

These are frequently prepared by the method just described for making tablet triturates. They consist of medicinal substances (intended to be administered subcutaneously) blended with a substance known to be completely soluble and inert. For this purpose sodium sulfate has been used, but now sugar of milk, especially that from goats' milk, is preferred. Most of the hypodermic tablets are now made by compression. Quick solubility and accuracy of dose are prime requisites in their manufacture.

TROCHES

Troches or lozenges are disklike masses of medicinal substances intended to be administered by slowly dissolving in the mouth. By reason of the method of administration the application of troches is limited to two classes of medicinal substances—first and usually, for the administration of medicines intended for application to the throat, and, secondly, in the administration of fairly mild and tasteless medicines in a palatable form. Since they are administered by slowly dissolving, no intensely bitter medicine should be used in the drug. Thus, to prepare troches of quinine sulfate would be scarcely short of senseless. A tasteless lozenge of quinine can, however, be made, and is described farther along.

Troches are manufactured in two ways—by massing and by compression. In making a lozenge by massing, the medicinal substances are combined with some mucilaginous substance, usually gum tragacanth, and moistened with sufficient water to make a mass, and are then worked up in a mortar similar to making a pill mass. When the mass is formed, it is rolled out with an ordinary biscuit roller on the biscuit board or pill tile, and from this rolled-out mass the lozenges are cut with an appropriate cutter. The details of the manufacture of such a mass will be found on page 353 in the discussion of the manufacture of lozenges of potassium chlorate. The apparatus required, as mentioned above, is a biscuit board, which, however, in the writer's experience, is not as satisfactory (by reason of the warping of wood) as a glass plate, or, in making small quantities, a pill tile. For rolling out the mass any ordinary rolling-pin will answer, the size depending upon the number of troches intended to be made. As to the lozenge cutters, they are generally hollow cylinders of tin tipped with steel, as shown in Fig. 234. The shape of this can be either round or hexagonal. Special forms of lozenge cutters for cutting six at a time have been devised (see Fig. 235).

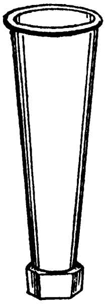


Fig. 234.—Lozenge cutter.

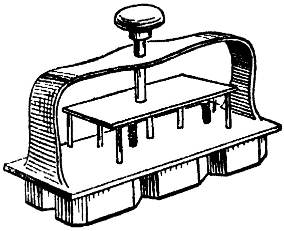


Fig 235.—Sixfold lozenge cutter.

The making of lozenges by compression is similar to making compressed tablets, the only difference being in the size of the mold. In the case of compressed tablets, the die arranged for 1-grain masses has a diameter of ¼ inch; while the 5-grain die is ⅜ inch in diameter. The lozenge being usually larger, a special die is provided, with all compressed tablet machines, in which the diameter is ½ to ¾ inch. Such a die is attached to the tablet machine, the powdered constituents blended in the proper way and compressed.

For throat troubles the compressed lozenges are even more valuable than massed lozenges, because in such cases the medicinal ingredients of these lozenges act best when they are slowly dissolved.

BACILLI

These are special forms of lozenges, consisting of cylinders about an inch in length and 1/8 to 1/4 inch in diameter. The best illustration of bacilli are the black licorice lozenges so largely sold in America these days. Such bacilli are made by taking the mass and either rolling it into a cylinder by hand and dividing on a pill-cutting machine, or, better still, forcing it through a bougie machine (p. 357), from which it emerges as a narrow cylinder which is cut by a knife into short pieces.

The only remaining official troches are the troches of elm. While N.F. IV gave recipes for 9 troches, N.F. V recognized only two and the N.F. VI has reduced this to one. Of the troches recognized by N.F. IV, five—charcoal, phenolphthalein, santonin, santonin compound, and sulfur and potassium bitartrate—were transferred in N.F. V to the class of tablets.

Trochisci Ulmi (N.F. VI) or *Troches of Elm*. Elm (20 Gm. per 100 troches), tragacanth, and sucrose in No. 80 powder are mixed. Anethol is then incorporated and a mass is made with water. Divide and dry in a current of warm air. *Dose*.—1 troche.

Trochisci Acidi Tannici (U.S.P. X) or *Troches of Tannic Acid* are made from tannic acid (6 Gm. per 100 troches), powdered sucrose, powdered tragacanth, and orange flower water by triturating the powders together, massing and dividing.

Trochisci Ammonii Chloridi (U.S.P. X) or *Troches of Ammonium Chloride* are made from ammonium chloride (10 Gm. per 100 troches), powdered extract of glycyrrhiza, powdered tragacanth, powdered sucrose, and syrup of tolu by mixing the powders and massing with the syrup and dividing.

Trochisci Cubebæ (U.S.P. IX) is made triturating together powdered extract of glycyrrhiza, acacia, oleoresin of cubeb (2 Gm. to 100 tablets) and oil of sassafras, massing with syrup and dividing the mass into troches.

Trochisci Potassii Chloratis (U.S.P. IX) are discussed on page 353. These lozenges must not be confounded with the compressed *tablets of the potassium chlorate*, which usually consist of 5 grains of that chemical in compressed form.

In making the troches, great care should be taken in mixing the potassium chlorate with the sugar, that combination, as mentioned on p. 468, being apt to explode. Not only is caution required in the manufacture, but also it is well to warn the purchaser that these lozenges should not be subjected to any violent concussion, as such is apt to produce a dangerous explosion. The dosage of these troches should be regulated.

Trochisci Sodii Bicarbonatis (U.S.P. IX) are made by triturating together freshly grated nutmeg, sucrose (sugar) and sodium bicarbonate (18 Gm. to 100 troches) massing with mucilage of tragacanth and dividing the mass into troches. These troches are now replaced by *Tabellæ sodii bicarbonatis* (N.F.). See p. 349.

Trochisci Eucalypti Gummi (N.F. V) or *Troches of Red Gum*, are made by triturating together powdered eucalyptus gum (6 Gm. to 100 troches), tragacanth, acacia, sucrose (sugar), oil of orange and fluidextract of rose; massing with water; and dividing the mass into troches.

In England, lozenges enjoy far more popularity than they do in this country and there are several types not described in either the Pharmacopœia or in the National Formulary.

Among these are *jujube paste lozenges*. The original jujube paste was prepared from the fruit of *Zizyphus jujube*, but it has long since been replaced by a base consisting of acacia, 18; sugar, 6; water, 80; evaporated on a water bath to 30 parts. With this base various medicines can be incorporated, and lozenges so prepared have been highly recommended by throat surgeons.

"Glyco-gelatin" lozenges are also very popular in England. These are made from a base which is prepared by soaking 1 ounce of gelatin in 2½ ounces of orange flower water until "jellified." To this is then added 2½ ounces of glycerin and enough carmine solution to color it. Gentle heat is then applied until the mass is fluid when it is poured into molds. Of course, various medicines can be added to the base, while it is fluid.

Chloroform lozenges are quite popular. These can be prepared by mixing together 3.5 cc. of chloroform, 0.5 cc. of oleoresin of cubeb, 1 cc. of tincture of capsicum, 0.3 cc. of oil of anise, 5 Gm. of powdered extract of glycyrrhiza, 3 Gm. of powdered acacia, 5 Gm. of powdered elm and 82 Gm. of powdered sugar. The mixture is then beaten into a mass by addition of water and divided into 100 troches.

These lozenges lose their chloroform by evaporation in a comparatively short time, but when extract of licorice is used as a diluent, the chloroform remains for a longer time. The tincture of capsicum is added to bring out the cooling action of the chloroform.

LABORATORY EXERCISES

MAKE LOZENGES OF POTASSIUM CHLORATE

Recipe.—Potassium chlorate, in fine powder	1.8 Gm.
Sugar, in fine powder	7.2 Gm.
Tragacanth, in fine powder	0.36 Gm.
Water, a sufficient quantity.	
To make	12 troches

Mix the sugar with the tragacanth by trituration in a mortar; then transfer the mixture to a sheet of paper, and by means of a bone spatula mix with it the potassium chlorate, being careful to avoid unnecessary trituration or pressure which might cause the mixture to ignite or explode. Lastly, form a mass with water and divide into 12 troches.

Remarks on Process.—The recipe just given is similar to but not identical with that given in U.S.P. IX.

Beware of trituration of dry potassium chlorate with sugar or other oxidizable substances, as a frightful explosion is apt to occur. Hence the direction that these ingredients be mixed on paper with a bone spatula. A metallic spatula can be used, however, if one is cautious in the manipulation.

Working the powders into a mass can be safely done with mortar and pestle, provided the mass is well moistened. Do not use too much water, however, lest a very soft mass results—1 cc. should suffice.

Roll out the mass as if it were biscuit dough, but do not roll too thin. In making 12 lozenges the mass is generally rolled out broad enough comfortably to cut 8 lozenges. The scraps are then worked up and rolled out so that 3 lozenges can be cut, and the scraps now remaining should be just enough to make the twelfth lozenge—no more, no less.

Both pills and lozenges should be air dried before putting away. If bottled while moist, they will grow moldy.

BIBLIOGRAPHY

Mass of Copaiba.—Kemp., Ph. Jl., 16, 1857, 546; Maisch, A.J.P., 35, 1863, 13.

Mass of Mercury.—Renodaeus-Uffenbachius, Dispensatorium, 1631, 447.

Confections.—Simon, Ph. Jl., 107, 1921, 519.

Confection of Damocratis, Rudolph, C.U.C.P., Alumni, Jl., 23, 1916, 61.

Pills.—(Manufacture) Rice, Am. Dr., 14, 1885, 191; Anon., Ph. Jl., 84, 1910, 399; Carles, A.J.P., 56, 1908, 106; Patch, Am. Dr., 15, 1886, 5 and 18, 1889, 39; Greenish and Pearson, Ph. Jl., 107, 1921, 495. (Disintegration) Trunkel, Ph. Zt., 76, 1931, 567. (Friable pills) Upjohn, U.S. Pat. 312041 (1885); Hallberg, West. Dr., 19, 1897, 93.

Pill Excipients.—Fantus, Jl. A.M.A., 86, 1926, 1129; Weinreich, Schw. Apoth. Zt., 63, 1925, 535; Schnellbach, A.J.P., 101, 1929, 137.

Coating Pills.—(General) Rice, Am. Dr., 15, 1886, 7; Wilbert, A.Ph.A., 56, 1908, 1061; Anon., Ph. Jl., 84, 1910, 424. (Gelatin) Vee, Jl. de. ph., 26, 1840, 585; Stevens, N.R., 12, 1883, 199. (Sugar) Grosh, A.Ph.A., 59, 1911, 106; Archibald, A.J.P., 39, 1867, 199; Rose, *ibid.*, 97, 1925, 71. (Chocolate) Fuller, Jl. Ind. Eng. Ch. 3., 1911, 254; Rose, A.J.P., 96, 1924, 590. (Tolu) Bukey and Brew., Jl. A.Ph.A., 24, 1935, 291.

Enteric Pills.—(Keratin) Unna, A.Ph.A., 33, 1885, 360; Puckner, Rep. Lab. A.M.A., 4, 1912, 121. (Salol) Byrd, Am. Dr., 47, 1905, 10; Peacock, Jl. A.Ph.A., 4, 1915, 947; (Stearic Acid) Toplis, Proc. P.P.A., 38, 1915, 262; Freeman, Ph. Jl. 120, 1928, 412. (Shellac) Wruble, A.J.P., 102, 1930, 318. (Enteric capsules) Scoville, Jl. A.Ph.A., 4, 1915, 1241; Volweiler, U. S. Patent 1,690,760; Weyland, Apoth. Zt., 46, 1931, 470.

Blaud's Pills.—Lundin, Svensk, Farm. Tid., through C.A., 11, 1917, 2261.

Lady Webster's Pills.—(History) Rudolph, Dr. Circ., 59, 1915, 295.

Pills of Phosphorus.—Dyer and Melville, Ph. Jl., 115, 1925, 145 and 179.

Compound Cathartic Pills.—Wood, A.J.P., 3, 1832, 207.

Compressed Tablets.—Brockedon, Brit. Pat. 9977 (1843); Kebler, Jl. A.Ph.A., 3, 1914, 820 and 937; Woolcock, Ph. Jl., [4], 80, 1908, 249; Mosley, Merck's Rep., 20, 1911, 70; Fantus and Snow, Jl. A.Ph.A., 5, 1916, 147 and 10, 1921, 850; White, *ibid.*, 9, 1920, 788; Williams, Dr. Circ., 65, 1921, 184; Foote, Bull. Univ. Wisc. No. 1566, Dec., 1928, 164 pages; Thoenessen, Dr. Circ., 73, 1929, 472; Thomann, Ph. Acta Helv., 5, 1930, 11, 17 and 95; Thieme, Apoth. Zt., 45, 1930, 37 and 133; Oberhard and others, Ph. Jl., 126, 1931, 233; Kampf, Ph. Acta. Helv., 10, 1935, 195.

Bichloride Tablets.—Raubenheimer, Jl., A.Ph.A., 3, 1914, 1158; Beringer, A.J.P., 86, 1914, 313; Levy, Jl. A.Ph.A., 5, 1916, 1229; Phillips, C.A., 14, 1920, 3472.

Tablet Triturates.—Fuller, Am. Dr., 16, 1887, 1; Fairhorn, A.J.P., 53, 1881, 397; Linhart, Dr. Circ., 55, 1911, 124.

Troches.—Rice, Am. Dr., 15, 1886, 21; Beringer and Kresge, Dr. Circ., 54, 1909, 361. (Jujube paste) Judd, A.Ph.A., 48, 1900, 535; Anon., Pract. Drug.; 39, June, 1920, 36; Robb, Ph. Jl., 105, 1920, 187. (Glycogelatin) Wokes, Am. Dr., 19, 1890, 48. (Chloroform lozenges) Beringer and Kresge, see above; Dowzard, A.J.P., 80, 1908, 511.

Candy Medication.—Fantus, Jl. A.Ph.A., 2, 1913, 778.

CHAPTER XX

SUPPOSITORIES

Suppositories are solid bodies intended to introduce medicinal substances into the various orifices of the body. The medicament is incorporated in a base that melts at body temperature. The Pharmacopœia gives general formulas for manufacture of suppositories with oil of theobroma and with glycerinated gelatin and this should be carefully read by the student.

SUPPOSITORIA—Suppositories

Under this heading the present Pharmacopœia prints a monograph discussing suppositories, their uses, their manufacture and their shape. The information given may be summarized as follows:

Suppositories are administered by inserting into rectum, vagina, or urethra, and according to place of insertion and material from which made, they are of different sizes and shapes, as tabulated below:

OFFICIAL SUPPOSITORIES

Application	*Shape*	*Weight*
Rectal.	Tapered.	2 Gm.
Urethral (bougies).	Pencil shaped.	2 to 4 Gm.
Vaginal.	Globular or oviform.	5 Gm.

Oil of theobroma suppositories can be made by fusion (p. 357) by massing (p. 358) or by cold compression (p. 358). In making suppositories containing phenol, hydrated chloral or other material which tend to soften the oil of theobroma, the addition of from 10 to 15 per cent of spermaceti is permissible. The melting point of the finished suppository must not, however, be above 37° C.

Glycerinated gelatin suppositories are made by dissolving or mixing the medicine with glycerin, combining this with fused glycerinated gelatin and then pouring into greased molds. For details see U.S.P., p. 369.

The ideal suppository consists of medicine blended with some inert base which will not liquefy at ordinary temperatures, but will melt at the temperature of the human body. The best substance adapted for this purpose is oil of theobroma (butter of cacao); that is, the official solid fatty oil, which, as is explained on p. 734, is a hard, firm mass, which, however, melts to an oily liquid at 90° to 95° F. In America practically all suppositories are made from this substance, its use having been suggested by A. B. Taylor, in 1852. In England glycerinated gelatin is popular as a suppository base, but this base possesses the decided disadvantage that the choice of medicinal ingredients to be blended with it is somewhat limited. Thus, under no circumstances should tannin or tannin-bearing drugs be combined with gelatin, for if this is done, an insoluble tannate of gelatin (leather) is formed.

A third suppository base, used only in one case, and that an official illustration, is the solidification of glycerin by means of stearic acid. This will be discussed in considering the official glycerin suppositories.

Manufacture of Suppositories.—There are three important ways of making suppositories—by *rolling*, by *molding*, and by *compressing*.

Of these processes, manufacture by rolling, that is, making into a mass, rolling out, cutting cylinder, and finally shaping by hand, and also by molding (or fusion), are outlined in above general directions, while minutiæ of each process, applied in special cases, are given on p. 358.

At this place it is, therefore, only necessary to say a few words concerning the apparatus (molds) used in preparing suppositories by fusion.

The suppository base is fused, the medicaments are added thereto, and the fused and well-stirred mixture is then poured into the thoroughly-chilled molds. Smith, Rae, and also Bateson point out the difficulty in obtaining a thorough admixture of the medicaments (especially heavy chemicals) in the finished suppositories. The writers suggest methods of manipulation which should be read in the original articles mentioned in the bibliography at the end of this chapter.

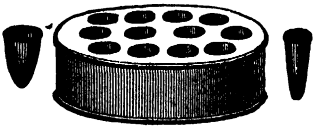


Fig. 236.—Individual suppository molds.

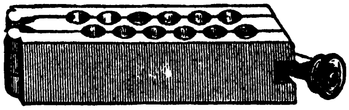


Fig. 237.—Divided suppository mold.

Suppository molds are made of brass, usually nickel plated, and are to be thoroughly chilled before the suppository mass is placed therein.

The first form of the suppository mold was the individual mold, consisting of a conic piece of steel hollowed out to the shape of a suppository, and a set of these molds is fitted into an appropriate holder which can then be immersed in ice-water, or a mixture of ice-water and salt, as shown in Fig. 236. These molds are absolutely useless in the modern pharmacy, there being no way of opening them to remove a possibly refractory suppository; and, moreover, the quantity of metal in the mold is not sufficient to insure a thoroughly uniform chilling. If such is used, the one way of removing the suppository is by tapping the mold, and if the mass sticks to the mold, nothing can be done except to dig it out by means of a wire or a file.

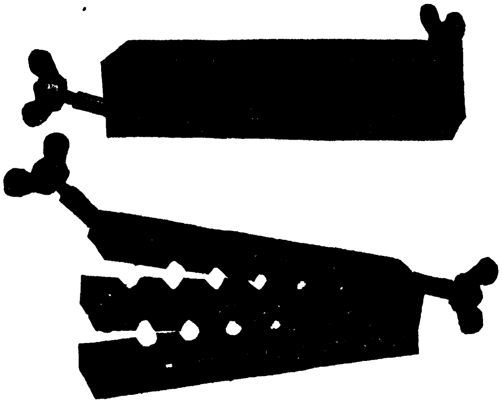


Fig. 238.—Benton-Hall suppository mold.

Divided molds consist of larger pieces of steel containing orifices for 6, 12, 24, or even a larger number of suppositories, so that they can be taken apart, thus dividing the mold in two pieces, as shown in Fig. 237. While being used, the two pieces are held together by means of clamps or pegs. Such molds are the most satisfactory that can be used, and if they have been left on the ice long enough to insure thorough chilling, the manufacture of suppositories with such molds yields most satisfactory results.

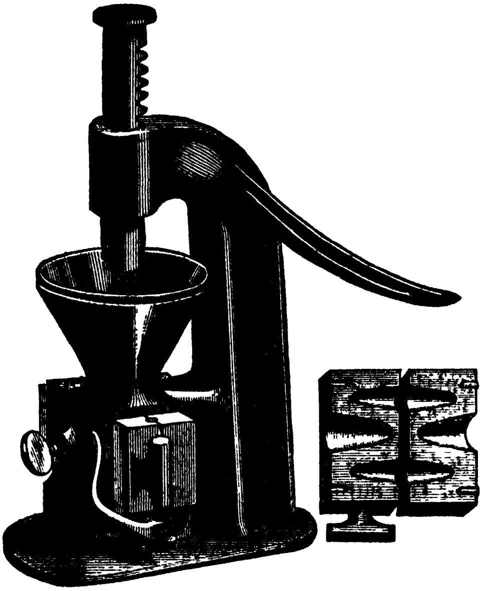


Fig. 239.—Suppository compressor.

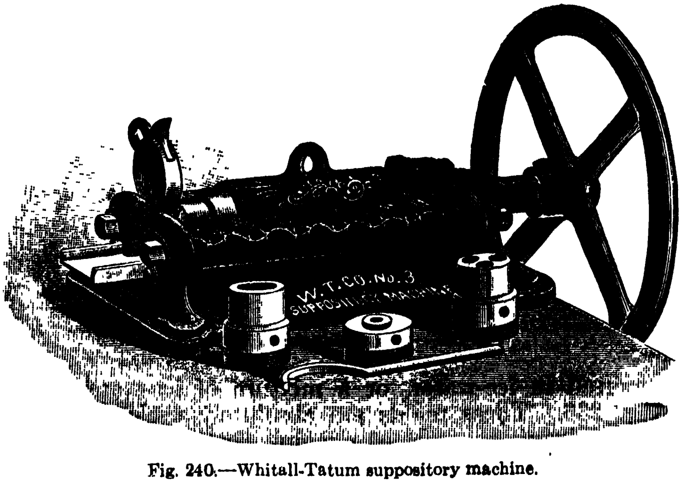


Fig. 240.—Whitall-Tatum suppository machine.

Quite a number of makes of divided suppository molds are on the market, and none of them is better than the hinged Benton-Hall mold, as shown in Fig. 238. It will be seen from the figure that this is on the same principle as the divided molds just described, but has the advantage of having a set of orifices at both top and bottom.

Suppositories by compression are made by mixing the medicinal substance with finely grated oil of theobroma and compressing it into the mold by means of appropriate leverage. Several varieties of such compressing machines are on the market. Earliest of these was the Archibald suppository machine (shown in Fig. 239), in which the mixture was passed through a funnel in which works a steel plunger, which forces the mass into a mold placed underneath the funnel. This form of suppository machine is not highly satisfactory, however, and is rarely used in these days.

The Whitall-Tatum suppository machine works far more efficiently. The cylinder is smaller and rests horizontally on the table rather than vertically (Fig. 240).

In making *bougies* by compression instead of the cone-shaped mold the mass is pressed through a die having a single but perfectly true cylindric orifice bored through it. The pressure of the plunger within the cylinder forces the mass through this narrow orifice, with the result of producing long, wormlike masses.

In lieu of compressing machines bougies can be made by working up the mass by hand and rolling it out as one would a pill cylinder. Or, if it is preferred to make the urethral suppository by fusion, the fused mass can be sucked up into a glass tube, which has been previously oiled.

The Pharmacopœia recognizes but one suppository by name.

SUPPOSITORIA GLYCERINI—Suppositories of Glycerin

(**Supp. Glycerin.**—Glycerin Suppositories)

Remarks.—The mass from which these suppositories are made is prepared by combining sodium stearate with glycerin at about 95° C., stirring until the sodium stearate is dissolved, adding distilled water and pouring into suitable molds. The cooled suppositories should be preserved in tightly-stoppered glass containers in a cool place. The preparation of the sodium stearate directly in the process of manufacturing the suppositories is permitted. This is accomplished by direct reaction of stearic acid and sodium bicarbonate, sodium carbonate or sodium hydroxide in correct proportion. The U.S.P. X directed manufacture of these suppositories from stearic acid and monohydrated sodium carbonate as outlined in the laboratory exercises below.

It is here necessary merely to call attention to the fact that a very small quantity (less than 10 per cent) of solids are able to solidify glycerin.

Suppositoria Boroglycerini (N.F.) or *suppositories of boroglycerin* are made by melting glycerinated gelatin and then adding to the fused mass glycerite of boroglycerin and glycerin. The mixture is then poured into molds. The suppositories contain 30 per cent of glycerite of boroglycerin.

LABORATORY EXERCISES

MAKE BELLADONNA SUPPOSITORIES

Extract of belladonna	0.32
Oil of theobroma	10.00

Make 5 suppositories.

Weigh the extract out on a piece of paper and transfer by means of a spatula to the point of the pestle, and made into paste with about 5 drops water in a warm mortar. In the meanwhile melt the oil of theobroma in small evaporating dish on water bath, and when completely fused, pour about one tenth of the oil into warm mortar containing the extract. Triturate until a complete blending of the oil and the extract takes place, and then transfer the still liquid mass into the rest of the oil of theobroma in the dish, carefully scraping all from mortar and pestle by means of spatula.

Mix the extract thoroughly with the molten oil of theobroma by stirring the glass rod, and remove from water bath, and when the first signs of congealing show, pour the mixture into the thoroughly chilled molds, keeping the extract suspended by constant stirring while pouring into mold. Then let mold stand quietly on the ice until solidification is complete, after which remove the suppositories from the mold.

Remarks.—The *extract* used in suppositories should be soft extract, not the powdered form.

Fusing the oil of theobroma should be at a low temperature. Heating too high gives the mass a fried smell.

Do not pour into molds while the mass is hot. Just before it congeals is the proper time.

Stir mass while pouring, else the extract will not be uniformly distributed.

Have molds on ice at least a half hour before pouring mass in. To get good results, the molds must be thoroughly chilled.

Have interior of molds perfectly dry and clean when mass is poured in. If such is the case, there is no need of using lycopodium to dust inside of mold.

The *mass, on congealing*, if molds are well chilled, contracts and loosens from molds with smooth, shining surface. In this case *suppositories can be removed from mold* by gentle tapping. If they stick, slight downward pressure from the top usually loosens them. If they stick more tenaciously, the molds must be cautiously opened and the suppositories removed by pressing from tip upward.

If the suppositories stick to mold, it is due either to insufficient chilling of molds before melted mass is poured in or to dirtiness of molds.

Most suppository molds hold 20 grains of oil of theobroma. This must be considered in making suppositories and the amount of oil of theobroma added in making the mass should be just enough to fill the molds.

MAKE SUPPOSITORIES BY HAND

Oil of theobroma	8 Gm.
Castor oil	q.s.

Grate or slice the oil of theobroma in thin shavings and put into mortar; add about 5 drops of alcohol and thus pulverize by intervention. Then add 5 drops of castor oil and work into mass as if making pills. Place finished mass on pill tile, dust with lycopodium, and roll out to mark 8 on scale on pill tile. Cut the cylinder in half and shape each half into a double cone by rolling gently with spatula. Then cut each double cone in half, and we have *four* suppositories.

Remarks.—This method does not yield as handsome a product as those made by fusion, but it has the advantage of being produced without special apparatus.

Avoid contact of the mass with the hand, as the oil of theobroma melts at temperature of the body.

In shaping the suppository, if found more convenient, the mass can be directly divided into 4 parts by measuring on pill tile or by weighing, and each part made into a cone.

These pure butter of cocoa suppositories are given merely for practice. Of course, in actual business, they will be directed blended with some medicinal constituents.

MAKE COMPRESSED SUPPOSITORIES

Take oil of theobroma q.s. (say 10 Gm.). Powder with alcohol, put into suppository machine, and press into both the rectal and the bougie mold. For picture of mold, see p. 355.

Remarks.—Note what is said just above as to fact that in actual business the oil of theobroma is always prescribed combined with some medicinal constituent.

MAKE GLYCERIN SUPPOSITORIES

Recipe.—	Glycerin	6.0 Gm.
	Monohydrated sodium carbonate	0.1 Gm.
	Stearic acid	0.4 Gm.
	Water	1.0 cc.
	To make	2 suppositories

Dissolve the monohydrated sodium carbonate in the water and add it to the glycerin, contained in a dish, on a water bath; add the stearic acid, and heat the mixture carefully until carbon dioxide ceases to be evolved and the liquid is clear. Then pour the melted mass into suitable molds, remove the suppositories when they are completely cold, and preserve them in tightly-stoppered glass vessels.

Remark on Process.—The recipe just given is similar to but not identical with that given in the U.S.P. X. The two recipes should be carefully compared by the student. The manufacture of these suppositories involves a chemical action, the sodium carbonate reacting with the stearic acid to form sodium stearate, and with this the glycerin blends, thereby producing a solid suppository containing about six sevenths its weight of glycerin.

Weigh the glycerin in small evaporating dish, and to it add the sodium carbonate and later the stearic acid.

Be sure the sodium carbonate is crystalline and monohydrated. The efflorescent salt works poorly.

Shave the stearic acid into thin pieces with knife or spatula before putting into glycerin.

Heat Carefully.—Experience shows, however, at this stage, that the heat of a water bath scarcely suffices, so when the sodium carbonate is dissolved, remove from water bath to wire gauze, dry the bottom of dish, and heat *very cautiously* until reaction ceases, *until escape of carbonic acid gas has ceased.*

Sodium carbonate plus stearic acid or any other acid gives off CO_2 gas, and forms a salt of the added acid.

Stir very slightly in making, and that only with glass rod, merely enough to aid the CO_2 in escaping. If stirred vigorously, the mass will become mixed with air and will not be clear.

The *mass must be clear* when poured into molds, else the finished suppositories will be opaque.

Pour Into Suitable Molds.—Note that the finished suppository will weigh over 3 Gm., about twice the ordinary rectal suppository. Hence the ordinary mold will not do. For practice, however, the mass may be poured into the smaller mold, thus making a suppository half the official size. In this case, as in belladonna suppositories, the mold must be thoroughly chilled by placing on ice, and the mass must be almost ready to congeal when poured in.

Removing these suppositories from the mold by tapping will not work; the molds must be opened and the suppositories removed by pressing from tip upward.

In place of ordinary suppositories there have been placed on the market the so-called *suppository capsules.* They consist either of a hollow mass of oil of theobroma, provided with a plug of the same material used to close the capsule; while others are made of gelatin, similar to gelatin capsules, only larger. In both cases the medicine intended to be administered as a suppository is supposed to be introduced into these capsules, which are then sealed and are then ready for insertion. It is hardly necessary to say that the careful pharmacist will avoid dispensing such suppositories. In the first place, one of the objects of using oil of theobroma mass is that the active medicinal ingredients shall be properly diluted, and to place these ingredients in such capsules, even though worked up with a small quantity of oil of theobroma, does not yield a suppository of a value equal to the one made by mixing the medicaments with the diluents.

Nasal coryza suppositories, consisting of a base of oil of theobroma in which has been incorporated antiseptics, such as oils of cassia, eucalyptus and thyme, phenol, camphor and menthol.

Politzer plugs are greased pellets of cotton about the size of a coriander seed with thread attached, for insertion in the ear as a protective.

BIBLIOGRAPHY

Suppositories.—(History) Wright, A.J.P., 42, 1870, 137. (Manufacture) Taylor, A.J.P., 24, 1852, 271; Rice, Am. Dr., 15, 1886, 127; Hocking and Brooke, Ph. Jl. [3], 20, 1890, 851; Dietrich, Am. Dr., 17, 1888, 226; Scoville, Dr. Circ., 49, 1905, 161; Smith, Quart. Jl. Ph., 2, 1929, 189; Rae, Ph. Jl., 121, 1928, 315; Bateson, *ibid.*, 121, 1928, 346.

Hollow Suppositories.—Smith, Quart. Jl. Ph., 2, 1929, 194.

Glycerol Suppositories.—Scoville, Jl. A.Ph.A., 13, 1924, 818.

Chloral Hydrate Suppositories.—Lewis and Dyer, Ph. Jl., 113, 1924, 88.

Nasal Suppositories.—Anon., Pacific Pharm., 3, 1910, 482.

Politzer Plugs.—Scoville, Art of Compounding, 1914, 231.

CHAPTER XXI

SOLID PREPARATIONS FOR EXTERNAL USE (CERATES, OINTMENTS, CATAPLASMS, PLASTERS, AND PAPERS)

CERATES

THESE are combinations of medicinal substances with fats and waxes intended to be used by spreading on cloth or paper, applying as one would a plaster. As the name suggests, cerates (from the Latin *cera*, wax) are supposed to contain wax, and a successful cerate should be soft enough to spread on cloth or paper, and yet thick enough not to become thin and oily in hot weather.

The fats used in the manufacture of cerates run the gamut of all available fatty substances. Lard is generally employed, but sometimes fatty oils are used; while in the present Pharmacopœia petrolatum and wool fat are prescribed in several cases. According to the amount of semisolid fat, such as petrolatum or lard, or of oil employed, the amount of wax required must be varied; oils, of course, requiring a larger amount. Again, in several recipes for cerates and ointments in the present Pharmacopœia, directions are given to use more wax in hot weather than during the cold weather.

The official cerates are made either by *fusion* or by *incorporation.* In the manufacture by fusion the constituent having the highest fusing point—say the wax—is usually heated first and to this when melted are added the other constituents such as lard or petrolatum. When completely fluid, the melted mass is strained through muslin into a mortar, and triturated until completely solidified. In incorporation the medicinal substance is placed on an ointment slab or in the mortar, and mixed with the fatty ingredients; in the first case, by rubbing with the spatula, and in the second, by trituration with the pestle.

In the present Pharmacopœia all three official cerates are made by fusion.

TABLE OF OFFICIAL CERATES
(ALL GALENIC AND ALL MADE BY FUSION)

Base	*Preparations*
White wax, and benzoinated lard	Cerate.
Yellow wax and lard	Rosin cerate.
Yellow wax, benzoinated lard and rosin	Cantharides cerate.
White petrolatum, white wax, and wool fat	Cerate of lead subacetate (N.F. VI).
Prepared suet, yellow wax, and rosin	Cerate of rosin compound (N.F. VI).

SPECIAL NOTES ON OFFICIAL CERATES

CERATUM—Cerate

(Cerat.—Simple Cerate)

Storage.—Preserve in a cool place.

Condensed Récipe.

Melt 300 Gm. white wax on a water bath, add 700 Gm. benzoinated lard; heat until all is liquefied, strain and then stir until solid. For details see U.S.P., p. 115.

Remarks.—This preparation, commonly called *simple cerate,* is made by the fusion of 30 per cent white wax, and 70 per cent benzoinated lard. The proviso in the U.S.P. X that the amount of wax may be varied to meet climatic conditions is omitted from the U.S.P. XI.

Simple cerate is rarely used except in combination with medicinal substances.

CERATUM CANTHARIDIS—Cantharides Cerate

(Cerat. Canthar.—Blistering Cerate)

Condensed Recipe.

Ingredients.—Cantharides in No. 80 powder, 350 Gm.; glacial acetic acid, 25 cc.; oil of turpentine, 150 cc.; yellow wax, 175 Gm.; rosin, 175 Gm.; benzoinated lard, 200 Gm.

Manipulation.—Macerate the cantharides with the oil of turpentine and the acetic acid in a warm place for forty-eight hours. Melt the rosin, wax and lard, add the cantharides mixture to the fused fat mixture and keep fused by heat of a water bath until the ointment weighs 1000 Gm. For details see U.S.P., p. 115.

Remarks.—This is prepared by macerating powdered cantharides with oil of turpentine and glacial acetic acid and mixing the other fatty constituents previously brought to fusion, keeping the mixture in a liquid condition for an hour. After the heat is removed the mass is stirred until cooled. The cantharides cerate is used for spreading what is commonly known as *fly blister*, this being the cerate spread on adhesive plaster in a layer about ¼ inch thick. This preparation is now given official recognition under the name, *cantharides plaster*. (See p. 377.)

CERATUM RESINÆ—Rosin Cerate

(Cerat. Res.—Resin Cerate)

Condensed Recipe.

Melt 350 Gm. rosin, add 150 Gm. yellow wax and 500 Gm. lard, heat until entirely fluid, strain and stir until solid. For details see U.S.P., p. 116.

Remarks.—This is best known by its synonym, *basilicon ointment.* It is made by the fusion of rosin, yellow wax, and lard, and it is worth noting that the U.S.P. X directed the changing of the proportion of the constituents according as the cerate is made in hot or cold weather. This proviso was eliminated in the U.S.P. XI.

The cerate has great popularity as a "drawing salve" for bringing boils "to a head."

Curatio Paraffini (N.F.) or *Paraffin Dressing* is cerate that is so hard that it has to be melted before application. It is made by fusing together paraffin, white petrolatum and olive oil and adding to the fused mixture a solution of resorcinol in oil of eucalyptus. This paraffin dressing is a war remedy resembling the French proprietary, *ambrine*, which enjoyed enormous popularity during the World War as an agent for healing burns and for restoring faces that had been disfigured by burns.

CERATES OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients. (figures show amount used in 100 Gm.)	Remarks.
Ceratum plumbi subacetatis.	Goulard's cerate.	Solution of lead subacetate, 20 Gm.; wool fat, white wax, white petrolatum; camphor, 2 Gm.	Was official in U.S.P VIII.
Ceratum resinæ compositum	Deshler's salve.	Rosin; yellow wax; prepared suet; turpentine; linseed oil.	Was official in U S.P. VIII.

OINTMENTS

Ointments are semisolid preparations containing medicinal substances blended with fatty matter of sufficient softness to permit their being applied to the skin by inunction. Ointments are always of softer consistence than are cerates, and have a lower melting point, less wax being used. Thus while *cerate* of the present Pharmacopœia contains 30 per cent white wax, the official ointment contains 5 per cent of white wax.

The choice of the *base* in making ointments is of much importance, since the medicaments contained in these preparations are supposed to be absorbed by the skin and if the base employed is not easily absorbed that result will not be obtained. Wool fat is supposed to be the base most quickly absorbed, goose grease and lard come next, while petrolatum is considered to be very slowly absorbed.

Hydrogenated oils (p. 727) are now recommended as ointment bases and Coppez states that petrolatum containing 3 per cent of cholesterol is an excellent substitute for wool fat in eye ointments. Rapp discusses ointments from the colloidal standpoint and gives high praise to the work of Moncorps. Rapp finds that the emulsion type of salves (cold creams) may be stabilized by the addition of pectin, cholesterol, and lecithin. The lecithin of soy bean is now available commercially at a reasonable price and serves admirably. Stern points out that in eczema ointments the pH of the salve should be close to that of the blood serum. Holmes finds that gum dammar is an excellent emulsifier (stabilizer) in the preparation of water in oil salves. The idea, however, is protected by U. S. patent, No. 1,429,430.

Gershenfeld and Miller suggest as bases for antiseptic ointments a combination of glycerin and *xerol* or *tegacid.* These two are trade names for glyceryl monostearate.

Ointments are manufactured either by *fusion* or by *incorporation.* In the fusion method, the fatty substances are liquefied by the aid of gentle heat, and the medicinal substances are incorporated either while the fats are liquefied or after solidification. In the case of the ointments made by incorporation the medicinal substances are rubbed up with solid fatty matter, either in a mortar or on an ointment slab. When pestle and mortar are used for the purpose of incorporation it is advisable to have the latter of a special flat shape, as shown in Fig. 241. An ointment prepared by fusion is usually finished by passing the fused mass through the strainer into a mortar, and triturating the mass until solidified. This has the effect of not only making the ointment smoother, but also lighter in color. In some of the ointments "whipping" is important in order to obtain a handsome product. Thus in making cold cream, the finished product is made light and fluffy by beating the mass with an egg-beater, and in making large quantities by working up in an emulsion machine (p. 285).

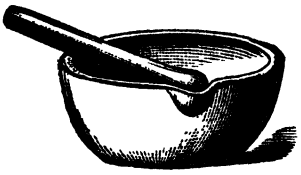


Fig. 241.—Ointment mortar.

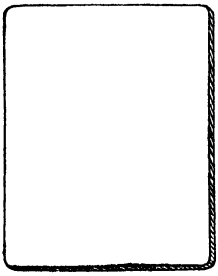


Fig 242 —Ointment slab.

In compounding prescriptions for ointments containing eutectic chemicals (p. 832) these chemicals should be triturated until liquefied and then incorporated in the ointment base.

When an ointment is prepared by incorporation on a slab, the apparatus needed consists of an ointment slab and a spatula. For the slab the ordinary pill tile can be used, although more handsome forms of slabs, made of plate glass, are obtainable (Fig. 242). Some years since, the use of pads of parchment paper was suggested instead of the slab, the idea being that, after the finishing of each ointment, the sheet of paper on which the ointment was worked up would be torn off and thrown away. This scheme, however, is not very satisfactory, inasmuch as in many cases it is advisable to triturate the chemicals incorporated in the ointment with considerable pressure, and the excuse for the use of the paper pad—saving the trouble of cleaning the ointment slab—was scarcely worth notice.

The spatulas used in incorporating ointments should be long and pliable, those made of nickel-plated steel being preferable. The iron spatula, however, can be used in all cases with those chemicals which will not attack iron, but must not be used in making citrine ointment (containing nitric acid) nor iodine ointment. For the latter purpose the steel spatula, coated with rubber, is very well adapted, although the objection to such rubber-coated spatulas is their tendency to peel. In preparing the ointment by incorporation on the slab the chemicals, which should be in a very fine divided form, are further subdivided by the process of levigation, using the end of the spatula blade in place of the muller, and a portion of the ointment base as the lubricator. In the making of the ointment of the red mercuric oxide the chemical is to be levigated with water with the rubber-coated spatula—in this case it being essential that the chemical be reduced to the finest possible form of powder. In manufacturing ointments on a large scale, paint mills or a special type of ointment mill, as shown in Fig. 243, are employed.

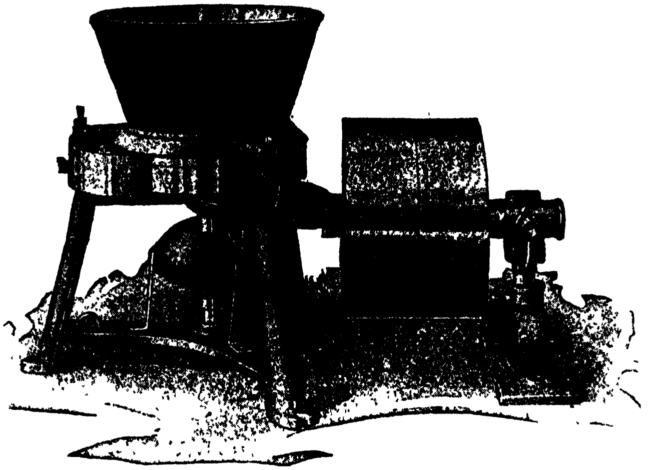


Fig. 243.—Stokes' power ointment mill

SPECIAL NOTES ON OFFICIAL OINTMENTS

UNGUENTUM—Ointment

(Ung.—Simple Ointment)

Condensed Recipe.

Melt 5 Gm. white wax on a water bath, add 5 Gm. of wool fat and 90 Gm. of white petrolatum, warm until entirely fluid, then stir until solid. For details see U.S.P., p. 415.

Remarks.—This preparation, commonly called *simple ointment*, is used almost entirely as a base for medicated ointments. This formula differs very materially from the simple ointment of the U.S.P. X which consisted of 20 per cent white wax and 80 per cent benzoinated lard. In the U.S.P. X permission was also given to increase the amount of wax employed, when climatic conditions render such a step advisable.

TABLE OF OFFICIAL OINTMENTS

(ALL GALENIC EXCEPT OINTMENT OF MERCURIC NITRATE AND STAINLESS IODIZED OINTMENT)

Process	*Base*	*Galenic preparations*	*Chemical preparations*
Fusion.	Lard.		Ointment of mercuric nitrate (N.F. VI).
	Lard and white wax.	Ointment of camphor (N.F. VI). Ointment of mustard (N.F. VI).	
	Yellow wax and petrolatum.	Pine tar ointment. Phenol ointment.	
	Yellow wax, petrolatum and wool fat.	Belladonna ointment. Ointment of calamine (N.F. VI). Chrysarobin ointment. Iodine ointment. Nutgall ointment. Ointment of resorcinol compound (N.F. VI). Tannic acid ointment. Yellow mercuric oxide ointment.	
	Yellow wax, lard and cottonseed oil.	Compound ointment of tar (N.F. VI).	
	Hydrous wool fat and white wax.	Compound ointment of menthol (N.F. VI).	
	Liquid petrolatum and white petrolatum.	Ointment of zinc stearate (N.F. VI).	
	Expressed almond oil, spermaceti and white wax.	Rose water ointment.	
	White petrolatum.	Ointment of lead oleate (N. F. VI).	
	White petrolatum and white wax.	Mild mercurial ointment.	
	White petrolatum, white wax and wool fat.	Ammoniated mercury ointment. Boric acid ointment. Ointment. Strong mercurial ointment. Ointment of potassium iodide (N.F. VI). Zinc oxide ointment.	
	White petrolatum, yellow wax and wool fat.	Sulfur ointment.	
	Petrolatum and paraffin.	Ointment of capsicum (N.F. VI).	Stainless iodized ointment (N.F. VI).
	Solid petroxolin.	Compound ointment of sulfur (N.F. VI).	
Incorporation.	Petrolatum.	Ointment of ichthammol (N.F. VI).	
	Petrolatum and wool fat.	Ointment of scarlet red (N. F. VI).	
	Petrolatum, wool fat and yellow wax.	Alkaline ointment of sulfur (N.F. VI). Ointment of red mercuric oxide (N. F. VI). Ointment of stramonium (N. F. VI).	
	White petrolatum and wool fat.	Compound ointment of benzoic acid (N.F. VI). Ointment of mild mercurous chloride (N.F. VI).	
	Paste of zinc oxide.	Ointment of coal tar (N.F. VI).	

UNGUENTUM ACIDI BORICI—Boric Acid Ointment

(Ung. Acid. Bor.—Boracic Acid Ointment)

Ointment of Boric Acid contains not less than 9 per cent and not more than 11 per cent of H_3BO_3.

Condensed Recipe.

Melt 5 Gm. white wax on a water bath, add 5 Gm. of wool fat, and 80 Gm. white petrolatum, heat until entirely fluid. Then pour little by little upon 10 Gm. powdered boric acid contained in a warm mortar, triturating until a smooth solid ointment results. For details see U.S.P., pp. 415 and 416.

Remarks.—This official contains 10 per cent of boric acid. The base has been changed from yellow wax and petrolatum of the U.S.P. X to white wax and white petrolatum. An assay process is given for determining the amount of boric acid. See U.S.P., p. 416.

UNGUENTUM ACIDI TANNICI—Ointment of Tannic Acid

(Ung. Acid. Tann.)

Caution.—During its manufacture and storage this ointment must not come in contact with iron utensils or containers.

Condensed Recipe.

Dissolve 20 Gm. tannic acid in 20 Gm. glycerin by use of gentle heat and then mix with previously melted yellow wax, 3 Gm.; wool fat, 3 Gm.: and petrolatum, 54 Gm. For details see U.S.P., p. 416.

Remarks.—This ointment is made by combining a glycerinic solution of tannin with the ointment base. Iron vessels must be avoided in its manufacture, since tannate of iron would form and the product would blacken.

UNGUENTUM AQUÆ ROSÆ—Rose Water Ointment

(Ung. Aq. Ros.)

Storage.—Preserve in pure tin, collapsible tubes.

Recipe and details of manipulation will be found below.

Remarks.—This popular face salve, commonly called *cold cream,* which is an emulsion of fat and waxes in a borax soap has the one drawback of rapidly turning rancid; hence the demand for a *theatrical cold cream* for use by actors for cleansing the face from paints, and which will keep perfectly.

This is solved by the substitution of liquid petrolatum for the expressed oil of almond in the official recipe, though it is needless to say such a cold cream should not be used in prescriptions.

LABORATORY EXERCISE

MAKE COLD CREAM

Recipe.—Spermaceti	6.25 Gm.
White wax	6.00 Gm.
Expressed oil of almond	28.00 Gm.
Sodium borate, in fine powder	0.25 Gm.
Stronger rose water	9.50 Gm.
To make about	50 Gm.

Reduce the spermaceti and the white wax to fine shavings, and melt them at a moderate heat; add the expressed oil of almond and stir, continuing the heat until the mixture is uniform; then gradually add the stronger rose water, previously warmed, and in which the sodium borate has been dissolved, stirring the mixture rapidly and continuously until it congeals and becomes of uniform consistence.

Remarks on Process.—The recipe just given is similar to but not identical with that given in the present edition of the Pharmacopœia which directs use of Rose Water U.S.P. plus oil of rose. The two recipes should be carefully compared by the student.

Melt the spermaceti and white wax in pint evaporating dish, and to the melted mixture add the oil of almond.

Dissolve the borax in the rose water in Erlenmeyer flask, and this solution should be almost as warm as the mixed fats. If it is cold, the spermaceti will separate as if curdled.

Do not warm the rose water enough to drive off its odor, however. The finished cold cream is not highly perfumed. If more odor is desired, add—

Oil rose	10 drops	to each pound
Oil lemon	6 drops	
Oil bergamot	4 drops	

The oils should be added, not alcoholic solutions of them.

This cold cream turns rancid quickly, and should, therefore, be sold only when fresh. For a permanent cold cream white paraffin oil is substituted for oil of almond. *This substitute must not, however, be dispensed as an official cold cream.*

UNGUENTUM BELLADONNÆ—Belladonna Ointment

(Ung. Bellad.—Unguentum Belladonnæ P.I.)

Belladonna Ointment yields not less than 0.118 per cent and not more than 0.132 per cent of the alkaloids of belladonna leaf.

Condensed Recipe.

Rub 10 Gm. pilular extract of belladonna with 5 cc. of diluted alcohol; triturate with a fused mixture of wool fat (5 Gm.), yellow wax (5 Gm.) and petrolatum (75 Gm.). For details see U.S.P., p. 417.

Remarks.—In preparing this ointment the wool fat is used to facilitate the absorption by the skin of the alkaloids of the extract. For assay see U.S.P., p. 418.

UNGUENTUM CHRYSAROBINI—Chrysarobin Ointment

(Ung. Chrysarob.)

Condensed Recipe.

Rub 6 Gm. chrysarobin with 6 Gm. liquid petrolatum and 4 Gm. chloroform; melt 5 Gm. wool fat, 5 Gm. yellow wax and 50 Gm. petrolatum on a water bath and add to chrysarobin mixture, triturating thoroughly; finally add petrolatum to make 100 Gm.

Remarks.—This process differs from the U.S.P. X method which required digesting chrysarobin in melted hydrous wool fat on a water bath for twenty minutes and then stirring until congealed.

UNGUENTUM GALLÆ—Nutgall Ointment

(Ung. Gall.)

Caution.—During its manufacture and storage this ointment must not come in contact with iron utensils or containers.

Condensed Recipe.

Incorporate 20 Gm. nutgall in No. 80 powder with a mixture of wool fat, 5 Gm., yellow wax, 5 Gm., and petrolatum, 70 Gm.

Remarks.—Like ointment of tannic acid, and for the same reason, metallic utensils must not be used in making this ointment.

UNGUENTUM HYDRARGYRI AMMONIATI—Ammoniated Mercury Ointment

(Ung. Hydrarg. Ammon.—White Precipitate Ointment)

Ammoniated Mercury Ointment contains an amount of ammoniated mercury corresponding to not less than 7.1 per cent and not more than 8.7 per cent of Hg.

Condensed Recipe.

Ingredients.—Ammoniated mercury, in No. 80 powder, 10 Gm.; white wax, 5 Gm.; white petrolatum, 80 Gm.; wool fat, 5 Gm.

Manipulation.—Rub the ammoniated mercury with the melted white petrolatum, wool fat, and white wax in a warm mortar, stirring until the mixture congeals.

Remarks.—In the U.S.P. X this ointment was made partly by fusion and partly by incorporation; that is, the ammoniated mercury was rubbed with liquid petrolatum and melted white petrolatum and then with unmelted hydrous wool fat.

UNGUENTUM HYDRARGYRI FORTE—Strong Mercurial Ointment

(**Ung. Hydrarg. Fort.**—Unguentum Hydrargyri Fortius U.S.P. X, Unguentum Hydrargyri)

Strong Mercurial Ointment contains not less than 48.5 per cent and not more than 51.5 per cent of Hg.

Condensed Recipe.

Triturate 500 Gm. mercury with 20 Gm. oleate of mercury. After standing fifteen minutes, add about 25 Gm. of a melted mixture of white petrolatum (130 Gm.), wool fat (300 Gm.), and white wax (50 Gm.) and triturate until the mercury is extinguished. Then add the rest of the melted mixture and mix well. For details and assay see U.S.P., p. 420.

Remarks.—Mercurial ointment is prepared on the same principle as blue mass, in that the mercury is finely divided and prevented from running together by coating each minute globule. In this ointment the mercury is extinguished with oleate of mercury and the globules are covered with wool fat and petrolatum; in short it is "water in oil" type of emulsion, the liquid, mercury, replacing the liquid, water, of the ordinary type of such an emulsion. Note that the globules must not be visible under a microscope magnifying ten diameters. Note that the present Pharmacopœia provides a mercury assay. (See U.S.P., p. 420.)

Jordan and Broady prepare a colloidal blue ointment by adding a solution of mercuric chloride to a solution of sodium hydroxide, gelatin, and formaldehyde. The moist colloidal precipitate is then incorporated in anhydrous wool fat and enough white petrolatum is then added to make the ointment of the required strength. By this procedure an ointment as strong as 60 per cent Hg. may be prepared.

Holdermann suggests a quick method of making mercurial ointment by starting in with a methyl alcohol solution of mercuric chloride mixing this with liquid petrolatum, adding an alkaline solution of formaldehyde, washing the mixture with water and finally adding to the mercury-petrolatum mixture enough wool fat to make a 30 per cent ointment.

Franklin suggests the use of 1.5 per cent of rosin in speeding up the extinguishing of the mercury.

UNGUENTUM HYDRARGYRI MITE—Mild Mercurial Ointment

(**Ung. Hydrarg. Mit.**—Diluted Mercurial Ointment, Blue Ointment, Unguentum hydrargyri P.I.)

Mild Mercurial Ointment contains not less than 28.5 per cent and not more than 31.5 per cent of Hg.

Condensed Recipe.

Mix 600 Gm. stronger mercurial ointment with 380 Gm. white petrolatum and 20 Gm. white wax previously melted together and congealed. For details see U.S.P., p. 421.

Remarks.—This officially gives pharmacopœial sanction to the custom of dispensing a 30 per cent mercurial ointment on calls for "blue ointment." It is commercially called "mercurial ointment ⅓." The use of petrolatum as a diluent is intentional, since the preparation is intended as an application for destroying body vermin and is not applied for the absorption of mercury through the skin. The assay process is similar to that for the stronger ointment.

UNGUENTUM HYDRARGYRI OXIDI FLAVI—Yellow Mercuric Oxide Ointment

(Ung. Hydrarg. Oxid. Flav.)

Caution.—During its manufacture and storage this ointment must not come in contact with iron utensils or containers.

Yellow Mercuric Oxide ointment contains not less than 0.9 per cent and not more than 1.1 per cent of HgO.

Condensed Recipe

Triturate 1 Gm. finely powdered yellow mercuric oxide with 1 Gm. liquid petrolatum to a smooth paste. Then incorporate with a mixture of melted wool fat, 5 Gm., yellow wax, 5 Gm., and petrolatum, 88 Gm. For details see U.S.P., p. 421.

Remarks.—In the U.S.P. X and XI, the strength of this ointment has been reduced from 10 per cent (U.S.P. IX) to 1 *per cent* strength. This ointment is now used almost exclusively for granulated eyelids and a 1 per cent *ophthalmic ointment* has almost entirely replaced the old 10 per cent preparation. As to the necessity of making a smooth ointment of yellow mercuric oxide, see p. 363.

UNGUENTUM IODI—Iodine Ointment

(Ung. Iodi)

Caution.—During its manufacture and storage this ointment must not come in contact with iron utensils or containers.

Iodine Ointment contains not less than 6.5 per cent and not more than 7.5 per cent of total I.

Condensed Recipe.

Dissolve 4 Gm. iodine and 4 Gm. potassium iodide in 12 Gm. glycerin and then incorporate with it, a melted mixture of yellow wax, 5 Gm.; wool fat, 5 Gm., and petrolatum, 70 Gm. For details and assay see U.S.P., p. 422.

Remarks.—The iodine in this preparation, as in the compound solution of iodine, is made soluble by the use of potassium iodide. A rubber-coated spatula should be used for mixing.

LaWall and Tice suggest an *antiseptic iodine ointment* made from 14 parts of a 7 per cent solution of iodine in dioxan (diethylene dioxide), 10 parts of paraffin, and 76 parts of white petrolatum.

UNGUENTUM PHENOLIS—Ointment of Phenol

(Ung. Phenol.—Ointment of Carbolic Acid)

Phenol Ointment contains not less than 1.8 per cent and not more than 2.2 per cent of C_6H_5OH.

Condensed Recipe.

Melt together, on a water bath, 2 Gm. phenol and 5 Gm. yellow wax; then add 93 Gm. petrolatum and stir until solid. For details and assay see U.S.P., p. 423.

Remarks.—This preparation is a 2 per cent mixture of phenol with yellow wax and petrolatum and is known as *ointment of carbolic acid.*

Reddish and Wales find that ointment of phenol and several other supposedly antiseptic ointments are not so in the modern sense of the word.

UNGUENTUM PICIS PINI—Pine Tar Ointment

(Ung. Pic. Pin.—Unguentum Picis Liquidæ)

Condensed Recipe.

Melt 15 Gm. yellow wax, then add 35 Gm. petrolatum and to the melted mixture, add 50 Gm. warmed tar; mix well, strain and stir until solid. For details see U.S.P., p. 423.

Remarks.—This ointment is of marked value in eczema and other skin troubles. It has however the objectionable property of staining the clothing.

UNGUENTUM SULFURIS—Sulfur Ointment

(Ung. Sulfur.)

Sulfur Ointment contains not less than 13.5 per cent and not more than 16.5 per cent of S.

Condensed Recipe.

Melt yellow wax, 5 Gm., on a water bath; add wool fat, 5 Gm. and white petrolatum, 75 Gm. When liquefied incorporate with precipitated sulfur, 15 Gm. For details and assay process see U.S.P., p. 424.

Remarks.—The ointment of the present Pharmacopœia contains just one half as much sulfur (15 per cent) as did the ointment of the Pharmacopœia of 1890.

UNGUENTUM ZINCI OXIDI—Zinc Oxide Ointment

(Ung. Zinc. Oxid.—Zinc Ointment)

Zinc Oxide Ointment contains not less than 19 per cent and not more than 21 per cent of ZnO.

Condensed Recipe.

Levigate 20 Gm. finely powdered zinc oxide with a mixture of wool fat, 5 Gm. and liquid petrolatum, 10 Gm. Melt together white wax, 5 Gm. and white petrolatum, 60 Gm., allow the mixture to cool and then thoroughly incorporate the zinc oxide mixture with the soft mass. For details and assay see U.S.P., pp. 424 and 425.

Remarks.—In order to make this ointment (*zinc salve*) perfectly smooth and absolutely free from grit it is necessary, first of all, that the zinc oxide be the pure official product, and not the gritty white zinc oxide which sells at low prices as a pigment. (See p. 537.)

The base of this ointment was changed in the revision of 1920 from unstable lard to the more stable petrolatum; dermatologists pointing out that as this ointment is applied almost solely as a protective covering, the nonabsorbability of the petrolatum is an advantage rather than otherwise.

Dispensing Ointments.—The finishing and dispensing of ointments and cerates is a matter requiring attention. In the first place, it should be borne in mind that the ointments, especially those made of benzoinated lard, have a tendency to become rancid, and such rancid ointments should never be dispensed; hence incorporated ointments should be prepared freshly as required. Nor should an ointment be dispensed containing the slightest quantity of grittiness, and to prevent this it is necessary to rub the medicinal substance thoroughly with a small quantity of the fatty matter before incorporating the entire amount. This applies particularly to the ointments containing such drugs as the yellow oxide of mercury, which is usually applied in cases of granulated eyelids. If any of the particles of mercuric oxide be still in the gritty form, it is sure to produce irritation. Hence the necessity of an absolutely smooth ointment.

As to the dispensing of the ointment, it should never be sent out in a wooden box unless the wood of which it is made is prepared so as to be impervious to grease. Even in dispensing small quantities of ointment over the counter a wooden box should never be used, as grease soon penetrates the wood, and the purchaser has a greasy package, which is an abomination. For small retail sales the pressed tin box (Fig. 244) should be used exclusively.

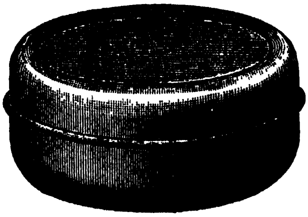


Fig. 244.—Tin ointment box.

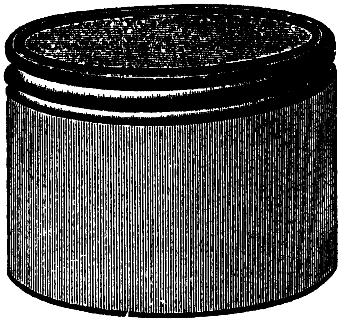


Fig. 245.—Ointment jar.

In dispensing ointments on prescriptions one of the several varieties of ointment jars (Fig. 245) should be used. These usually consist of a glass jar with a metallic or composition (Bakelite) cover fastening to jar by a screw joint. The cover is nickel plated or otherwise smooth and glossy and the label should therefore be pasted to the side of the glass jar. If it is desirable to use a rounded label on the cover, the form of ointment box shown in Fig. 246 should be used. When the label is placed on the side of the glass jar it invariably becomes greasy while in the cover just mentioned it is protected on top by a transparent sheet and underneath by cardboard impervious to grease, and the label will, therefore, remain fresh for a long time. A satisfactory way of dispensing ointments is in collapsible tubes (Fig. 247), made of tin free from lead. Such a tube is convenient for the

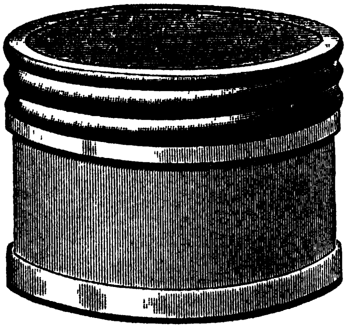


Fig. 246.—Ointment jar with mica top.

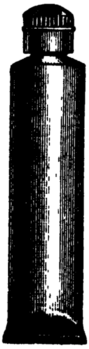


Fig. 247.—Collapsible tube.

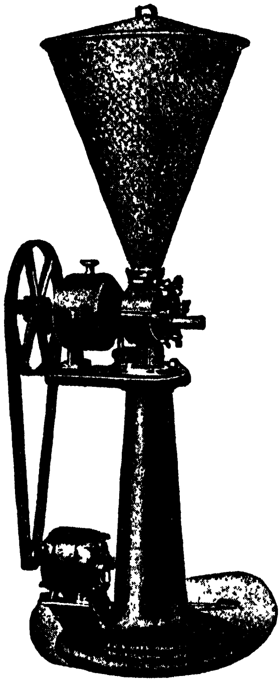


Fig. 248.—Stokes' tube filling machine.

person who expects to carry an ointment around with him. Filling such tubes is best done by rolling the ointment in waxed paper, slipping the roll into the tube and then, after pressing the paper firmly between thumb and forefinger of left hand slowly pulling the paper out with the right hand thus leaving the ointment in the tube. Special filling machines (Fig. 248) are now available for filling collapsible tubes on a large scale.

In this connection it might be well to cite a novel method of dispensing a mercurial ointment now in vogue, which consists in placing in soft gelatin capsules sufficient of the ointment for one rubbing, the set of capsules being carried around in a pill box in the vest pocket.

Old-time pharmacists, after placing the ointment in an ointment box, invariably "finished" them by ornamenting the surface exposed to the air with fanciful designs. These designs were made with specially cut pieces of tin (Fig. 249), which were held firm while the ointment in the jar was gradually rotating under it. This idea was admirable in showing the purchaser whether the ointment had been tampered with by the messenger, but is now rapidly becoming obsolete, the pharmacist and purchaser depending more on the external appearance of the package for signs of tampering.

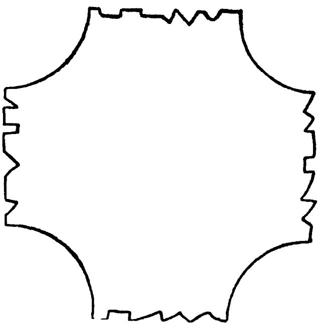


Fig 249.—Tin ointment finisher.

Preservation of Ointments.—Ointments should be stored in a cool place, preferably in a refrigerator.

Unguentum Ichthammolis (N.F. VI), known in the N.F. V as unguentum bituminis sulphonati (N.F.) is a 10 per cent ointment of ichthyol (p. 645).

Unguentum Hydrargyri Chloridi Mitis (N.F. VI) or *Prophylactic Ointment*, is a 30 per cent *calomel ointment*, now largely in vogue as a venereal prophylactic.

Unguentum Iodatum Denigrescens (N.F. VI) is a 5 per cent iodine ointment made up with oleic acid, paraffin, and petrolatum. The oleic acid combines chemically with the iodine (see iodine absorption number, p. 1025) and thus produces a so-called "iodine ointment" that does not stain the skin. Note that the N.F. calls it stainless *iodized* ointment and not *iodine* ointment. Zeigler finds that this preparation, while absorbable, does not possess antiseptic properties.

Unguentum Iodoformi (U.S.P. X) or *Iodoform Ointment* is made by triturating 10 Gm iodoform with 70 Gm. of melted petrolatum and 20 Gm. wool fat, added little by little. The odor of the iodoform can be removed from the mortar by burning alcohol therein (p. 286). How the odor may be partially masked is suggested under Iodoform.

Unguentum Plumbi Oleatis (U.S.P. X; N.F. VI) or *Ointment of Lead Oleate* is made by melting 50 Gm. lead oleate plaster with 49 Gm. white petrolatum, straining, adding oil of lavender and stirring until solid. This old-time preparation, usually called *diachylon ointment*, is lead plaster softened with white petrolatum and perfumed with oil of lavender.

Unguentum Solubile is an ointment base suggested by Stephan. This consists of a jelly made by triturating 3 Gm. of powdered tragacanth with 5 Gm. of alcohol, then adding 50 Gm. of glycerin and 42 Gm. of water Obviously this is not an ointment in the true pharmaceutical sense, since it contains no fatty matter. It is mentioned however at this place merely because it is called an ointment.

Unguentum Stramonii (U.S.P. IX; N.F. VI) is made by triturating pilular extract of stramonium (10 parts) with diluted alcohol (5 parts) and then with hydrous wool fat (5 parts); yellow wax (5 parts), and petrolatum (75 parts).

Oculenta is the name given by the British Pharmaceutical Codex to a class of ointments designed for the eye. In this connection, special attention should be called to the necessity of using extreme precautions in preparing eye salves. Not only should these preparations be dispensed absolutely free from gritty particles, but special precautions must be observed in preparing such ointments under aseptic conditions. Outstanding prescription pharmacies in the United States now have special glass-enclosed scrupulously clean compartments in which all eye prescriptions are compounded.

OINTMENTS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients. (figures show amount used in 100 Gm.)	Remarks.
Unguentum acidi benzoici compositum.	Whitfield's ointment.	Benzoic acid, 12 Gm.; salicylic acid; wool fat; white petrolatum.	
Unguentum calaminæ.	Turner's cerate.	Prepared calamine, 17 Gm.; yellow wax; wool fat; petrolatum.	Also called *unguentum zinci carbonatis crudi.*
Unguentum camphoræ.	Camphor ointment.	Camphor 22 Gm.; white wax; lard.	Called *pomade camphrée* in French speaking countries.
Unguentum capsici.	Capsicum ointment.	Oleoresin of capsicum, 5 Gm.; paraffin; petrolatum.	
Unguentum hydrargyri chloridi mitis.	Calomel ointment	....	See p. 371.
Unguentum hydrargyri nitratis.	Citrine ointment.	....	See p. 621.
Unguentum hydrargyri oxidi rubri.	Ointment of red mercuric oxide (U.S.P. VIII).	Red, mercuric oxide, 10 Gm.; liquid petrolatum; yellow wax; wool fat; petrolatum.	Also called *red precipitate ointment.*
Unguentum ichthammolis.	Ichthammal ointment	....	See p. 371.
Unguentum iodatum denigrescens.	Stainless iodized ointment.	....	See p 371.
Unguentum mentholis composiitum.	Analgesic balm.	Menthol, 15 Gm ; methyl salicylate; white wax; hydrous wool fat.	Inunctum mentholis compositum (N.F. V).
Unguentum picis carbonis.	Ointment of coal tar.	Coal tar, 5 Gm.; paste of zinc oxide.	
Unguentum picis compositum.	Compound tar ointment.	Rectified oil of tar, 4 Gm.; tincture of benzoin; zinc oxide; yellow wax; lard; cotton seed oil.	
Unguentum plumbi oleatis.	Unguentum diachylon.	Plaster of lead oleate, 50 Gm.; oil of lavender; white petrolatum.	
Unguentum potassii iodidi.	Ointment of potassium iodide (U.S P. VIII).	Potassium iodide, 10 Gm ; sodium thiosulfate; water; wool fat; white wax; white petrolatum.	Sodium thiosulfate used to decolorize iodine liberated from the iodide. Should be freshly prepared.
Unguentum resorcinolis compositum.	Compound resorcinol ointment.	Resorcinol, 6 Gm.; zinc oxide; bismuth subnitrate; rectified oil of birch tar; yellow wax; petrolatum; wool fat; glycerin.	Similar to the proprietary ointments containing resorcinol.
Unguentum rubri scarlatini.	Ointment of scarlet red.	Scarlet red, 5 Gm.; olive oil; wool fat; petrolatum.	
Unguentum sinapis.	Mustard ointment	Volatile oil of mustard, 2 Gm.; white wax; lard.	Similar to proprietary ointments containing mustard oil.
Unguentum stramonii.	....	....	See p. 371.
Unguentum sulfuris alkalinum.	Alkaline sulfur ointment.	Sublimed sulfur, 20 Gm.; potassium carbonate; water; wool fat; yellow wax; petrolatum.	
Unguentum sulfuris compositum.	Wilkinson's ointment.	Precipitated calcium carbonate; sublimed sulfur, 15 Gm.; juniper tar; soft soap; solid petroxolin.	Also called *Hebra's itch ointment.*
Unguentum zinci stearitis.	Ointment of zinc stearate (U.S.P.) VIII).	Zinc stearate, 35 Gm.; liquid petrolatum; white petrolatum.	

SOLID PETROXOLINS

In addition to the liquid petroxolins, those liquid petrolatum preparations resembling liniments (see p. 292), the National Formulary provides a recipe for solid petroxolin, which is a form of petrolatum ointment containing ammonium oleate.

Petroxolinum Spissum (N.F.) is prepared by melting together yellow wax and light liquid petrolatum, adding oleic acid to the mixture and triturating the fused fats in a warm mortar with a mixture of alcohol and stronger ammonia water. It is perfumed with oil of lavender.

INUNCTIONS

Inuncta are ointments, in which hydrous wool fat is the main fatty constituent. They contain medicaments intended to be quickly absorbed by the skin and in many cases are designed to produce local irritation. They resemble the "analgesic balsams" which are popular in Europe. Inunctions are best dispensed in collapsible tubes. The National Formulary V recognized Inunctum Mentholis made by incorporating menthol (5 per cent) in hydrous wool fat and Inunctum Mentholis Compositum. The former has been dropped from the N.F. VI and the latter is recognized under the title of *Unguentum Mentholis Compositum.*

Unguentum Mentholis Compositum (N.F. VI), listed in the N.F. V as Inunctum Mentholis Compositum, contains menthol (15 per cent), methyl salicylate (10 per cent), white wax, and hydrous wool fat.

DERMATOLOGIC PASTES

The National Formulary V recognized under the title *pastæ dermatologicæ* ointment-like mixtures of starch, dextrin, zinc oxide. sulfur, etc., made into a paste with glycerin, soft soap, petrolatum, lard or other fats. Recipes for 7 such pastes were given. The N.F. VI does not give a general monograph for these pastes and dropped 3 of those listed in the N.F. V but added 4 new ones to the N.F. VI. The eight official pastes are listed immediately below and the three dropped from the N.F. VI follow:

Pasta Acidi Acetylsalicylici Composita (N.F. VI) or *Dental Anodyne Paste*, made from acetylsalicylic acid, Peruvian balsam, and eugenol with a 10 per cent white wax and wool fat base.

Pasta Betanaphtholis (N.F. V) or *Lassar's Naphthol Paste*, made from betanaphthol (10 per cent), precipitated sulfur, petrolatum, and soft soap.

Pasta Bismuthi (N.F. VI) or *Beck's Bismuth Paste*, made from bismuth subnitrate (30 per cent), white wax, paraffin, and white petrolatum.

Pasta Dextrinata (N.F. V) a basic paste made from white dextrin, glycerin and water.

Pasta Resorcinolis Fortis (N.F. VI) or *Lassar's Stronger Resorcinol Paste*, made from resorcinol (20 per cent), zinc oxide, starch, and light liquid petrolatum.

Pasta Resorcinolis Mitis (N.F. VI) or *Lassar's Mild Resorcinol Paste* made like the foregoing except that the resorcinol content is 10 per cent.

Pasta Zinci Oxidi Mollis (N.F. VI) or *Unna's Soft Zinc Paste*, made from zinc oxide (25 per cent), precipitated calcium carbonate, oleic acid, linseed oil, and lime water.

Pasta Zinci Oxidi (N.F. VI) or *Lassar's Plain Zinc Paste*, made of zinc oxide (25 per cent), starch, and white petrolatum.

Pasta Zinci Oxidi cum Acidi Salicylico or *Lassar's Zinc Paste with Salicylic Acid*, made from salicylic acid (2 per cent) and Pasta Zinci Oxidi.

Pasta Zinci Oxidi Dura or *Unna's Hard Zinc Paste*, made from zinc oxide (25 per cent), purified siliceous earth and benzoinated lard.

Pasta Zinci Sulphurata (N.F. V) or *Unna's Sulfurated Zinc Paste*, made from zinc oxide (15 per cent), precipitated sulfur, purified siliceous earth, and benzoinated lard.

Unna recommends in certain cases where a protective coating containing medicinal substances is indicated, *casein varnishes*. According to Hager such a varnish or paste can be made either by digesting 5 Gm. of casein with 0.6 Gm. of borax and 25 Gm. of water or else 1 part of casein is dissolved in 3 parts of 25 per cent ammonia water, the solution mixed with 1 part of glycerin and heated on a water bath until the excess of ammonia is driven off, after which 2 parts of boiling water are added to the residue and triturated until a smooth paste results.

MULLS OR STEATINS

These are ointments of high fusing points, containing the desired medicinal agents and spread on soft muslin or "mull." The National Formulary V gave a general formula for mulls, under the title *Mullæ* in which the method of spreading is described at some detail. It also listed the following special mulls. However, these have all been dropped from the N.F. VI.

Mulla Acidi Salicylici (N.F. V) made by mixing salicylic acid (10 per cent) with benzoinated lard and benzoinated suet.

Mulla Creosoti Salicylata (N.F. V) made from salicylic acid (10 per cent), creosote (20 per cent), yellow wax, and benzoinated suet.

Mulla Hydrargyri Chloridi Corrosivi (N.F. V) made by dissolving corrosive mercuric chloride (0.2 per cent) in alcohol and mixing the solution with benzoinated lard and benzoinated suet.

Mulla Zinci (N.F. V) made by mixing zinc oxide (10 per cent) with the fats just mentioned.

GLYCEROGELATINS

These are soft masses containing medicinal substances used in dermatological practice made with glycerinated gelatin U.S.P. as a vehicle. They are firm enough to be molded and yet melt at the body temperature. The National Formulary VI gives a general formula for making these products but dropped the 4 special formulas listed in the N.F. V.

The general formula is as follows: Glycerinated gelatin, 30 Gm.; glycerin, 25 Gm.; distilled water, 35 cc., and the medicinal substance, in fine powder, 10 Gm. Mix the medicinal substance with glycerin or dissolve it, add the water and incorporate with the melted glycerinated gelatin; pour into chilled molds. The amount of glycerinated gelatin may be varied to control the melting point.

Glycerogelatinum Acidi Salicylici (N.F. V) is made by fusing glycerinated gelatin, glycerin, distilled water, and salicylic acid (10 per cent) and then pouring the homogeneous mixture into chilled molds.

Glycerogelatinum Iodoformi (N.F. V) contains in molded form, glycerinated gelatin, glycerin, distilled water, and iodoform (10 per cent).

Glycerogelatinum Zinci Durum (N.F. V) contains in molded form, glycerinated gelatin, glycerin, distilled water, and zinc oxide (10 per cent).

Glycerogelatinum Zinci Molle (N.F. V) differs from the foregoing *firm zinc glycerogelatin*, only in the proportion of glycerinated gelatin and glycerin. In the firm glycerogelatin the proportion is 30 to 25; in the soft variety it is 20 to 35.

PASTE PENCILS

Stili Medicamentorum (N.F. V), or *stili dilubiles*, or *Unna's pencils* are prepared by incorporating the medicinal agent (something used in dermatology) with a paste consisting of starch and other adhesive materials. The mass is rolled into thin cylinders (about 1/5 inch in diameter) as in making pills and then cut into sections about 2 inches long and after drying, each pencil is wrapped in tin foil.

Stili Acidi Salicylici Dilubiles (N.F. V) or *salicylic acid pencil*, the mass of which contains salicylic acid; (10 per cent) tragacanth, starch, white dextrin, and sucrose (sugar). Distilled water is used as the excipient. Each pencil will weigh slightly over 2 Gm.

This class of preparations was dropped completely from the N.F. VI.

CATAPLASMS

Cataplasma or *poultices* are wet masses of solid matter applied to the skin for the purpose of reducing inflammation, or in other cases to act as counterirritants.

The solid matter used as the base is chosen with a view to its capacity to absorb water. Thus the base of the one official cataplasm is clay, while mucilaginous drugs, such as ground flaxseed, are valuable as poultice bases.

If the poultice is intended to reduce inflammation, the proper base is one devoid of medicinal action, and the poultice wet with cold liquid acts similarly to a cold compress (that is, a wad of cloth or cotton wet with water). If intended to act as a counterirritant, the poultice is either applied hot or is made from some drug possessing rubefacient properties. An illustration of the latter case is formed in the poultice made of ground mustard, which is replaced in the Pharmacopœia by the more elegant *mustard plaster* or *paper*.

The only cataplasm mentioned in either the Pharmacopœia or the National Formulary is:

Cataplasma Kaolini (U.S.P. VIII; N.F. VI) which consists of a mixture of kaolin, boric acid, and glycerin, flavored with thymol, methyl salicylate, and oil of peppermint, and which is similar to a popular proprietary preparation largely prescribed by physicians. It is indicated as a local application in a large number of inflammatory diseases, and is also of value as a mild antiseptic in minor wounds.

PLASTERS

Plasters are solid preparations containing medicinal substances intended to be applied to the skin, and of sufficient adhesiveness to adhere firmly. Plasters are different from cerates in being practically free from fats, and also in the fact that the cerates, when spread on cloth and applied, are not of sufficient adhesiveness to stick firmly to the skin, their removal being a very simple matter. Plasters, on the other hand, made of adhesive or resinous substances, stick very firmly to the skin; in fact, so firmly that it is sometimes a matter of difficulty to remove them.

As bases of plasters are used gum resins, lead plaster, resin plaster, Burgundy pitch, isinglass, and latterly, India rubber. In former years the first-named plaster bases were used quite extensively, but during the last twenty years machine-made plasters with rubber base have practically driven the old-fashioned type of plasters out of the market, so that now the pharmacist is very rarely called upon to dispense a pharmacopœial plaster, and the art of spreading plasters is rapidly becoming a lost one.

Before discussing the official plaster masses a few words regarding the manufacture of rubber plasters may not come amiss.

The original and really satisfactory India-rubber plasters are made by kneading crude rubber with resinous substances, such as gum olibanum, until a plastic mass results. This kneading is accomplished by rolling the rubber between two corrugated rollers washing it at the same time in a stream of water. The resulting sheets are then dried and are then run into the grinder consisting of two smooth rollers which softens the rubber to proper plasticity for admixture with the other ingredients. This is done by passing the mixture between rollers, one operating twice as fast as the other. By continued passage between these rollers a uniform mass finally results. The plaster mass is then spread on cloth by rolling between hot plates, both heat and pressure being required to spread it to the proper thickness. The modern rubber plaster base consists essentially of 30 per cent of rubber, 40 per cent of pitch, 20 per cent of zinc oxide, and 10 per cent of orris or starchy filler. The making of such rubber plasters requires powerful and expensive machinery, and scarcely had the rubber plaster manufacture been placed on a paying basis, before other and inferior methods were substituted for the original process. In the cheaper methods the rubber is dissolved in the appropriate solvent, usually benzin, and the solution evaporated down to the consistence of a soft extract; and when it is spread on cloth, the surplus benzin is permitted to evaporate.

Such plasters are in every way inferior to the machine-kneaded plasters; the cohesive property of the mass is less, and such a plaster, on removal from the back to which it has been applied, very frequently tears off, leaving patches of the plaster sticking to the skin.

The manufacture of pharmacopœial plasters may be divided into two parts: making the mass and spreading the same. The making of the official plaster mass is usually a matter of little difficulty, being generally prepared by fusing the various constituents or, in some cases, by softening them by gentle heat. The official plaster mass is then rolled into appropriate sticks, or left in the plaster dippers in which they have been fused, until a spread plaster is called for.

The spreading of a plaster is a matter calling for a high degree of skill and requiring much practice. For details of the spreading of a plaster see Laboratory Exercises on page 379. Suffice it to say here that the molten plaster mass is spread on plaster skin or cloth, the area, including the dimensions directed by the physician, being inclosed in strips of paper, the entire paraphernalia—the cloth or skin base and the paper—being firmly fastened to a perfectly level table or to a smooth board resting on the counter by means of thumb tacks. So soon as the molten plaster mass is poured upon cloth or skin base, it is spread by the rapid movement of a hot, clean spatula. If, in spreading, the hand trembles or the plaster mass is not warm enough to follow the spatula, an unsuccessful plaster results.

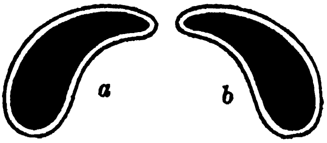


Fig. 250.—Ear plasters: *a*, For left ear; *b*, for right ear (Thornton).

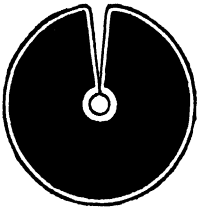


Fig. 251.—Breast plaster (Thornton).

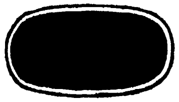


Fig. 252.—Kidney plaster (Thornton).

In former years there was considerable demand for specially shaped plasters, such as those to fit behind the ear, to cover the breast, or to place over the kidneys. These were spread on cloth by substituting for the plain paper strips above mentioned a pattern made of stiff paper, having cut out from its center the shape required for the plaster (Figs. 250, 251, and 252). The details of the spreading of the specially shaped plasters are exactly the same as for an oblong plaster.

In the old times, when plaster spreading flourished and numbers of plasters were called for in a day's prescription business, special apparatus was devised for spreading plasters by hand on a large scale. An example of these spreading machines is found in the plaster spreader, a picture of which is appended (Fig. 253).

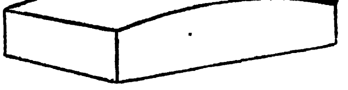


Fig. 253.—Plaster spreader.

At the present time there are few stores possessing such, the demand for hand-spread plasters being practically nil. Among the few survivors of hand-spread plasters are the so-called "fly blisters" (see below).

The decline in the manufacture of plasters by the pharmacist is strikingly shown in the handling of the subject in the present Pharmacopœia. In the Pharmacopœia of 1890, thirteen plaster masses were official, while in the U.S.P. X there were six plasters official, only three of which were supposed to be prepared by the pharmacist, the other three monographs describing the commercial finished plaster. The present Pharmacopœia lists only four plasters and the N.F. VI one. Of these two U.S.P. plasters are for preparation by the pharmacist and the N. F. plaster is the basic lead plaster used in making the lead oleate or diachylon ointment.

TABLE OF OFFICIAL PLASTERS

(All Galenic Except Lead Plaster)

Process	*Base*	*Preparations*
Plaster mass made by fusion.	Lead oleopalmitate.	Lead oleate plaster (N.F. VI).
Spread plaster.	Adhesive plaster.	Cantharides plaster.
Commercial ready-made spread plaster.	Rubber plaster.	Adhesive plaster.
		Belladonna plaster.
	Rubber solution spread on paper or cloth.	Mustard plaster.

SPECIAL NOTES ON OFFICIAL PLASTERS

EMPLASTRUM ADHÆSIVUM—Adhesive Plaster

(**Emp. Adhæs.**—Rubber Adhesive Plaster)

Adhesive Plaster is a mixture of rubber, resins, and waxes, with one or more fillers of absorbent powder, such as zinc oxide, orris root, or starch, mechanically mixed and spread evenly upon cotton cloth.

Each 100 square centimeters of the plaster contains not less than 1.5 Gm. of the plaster mass.

Remarks.—This official represents the *rubber sticking plaster* of commerce. The old-fashioned sticking plaster, *emplastrum resinæ* (U.S.P. IX) is becoming obsolete. Note that the official adhesive plaster should contain 30 per cent of rubber and 15 per cent of zinc oxide if that chemical is used as a filler. The plaster mass must be free from nodules and the cotton fabric backing must have not less than 31 warp threads per centimeter and not less than 31 filling threads per centimeter and must weigh at least 1.18 Gm. per 100 square centimeters.

EMPLASTRUM BELLADONNÆ—Belladonna Plaster

(Emp. Bellad.)

Belladonna Plaster is a mixture of adhesive plaster mass and an extract prepared from belladonna root, spread evenly upon fine cotton cloth or other suitable backing material. The plaster mass yields not less than 0.25 per cent and not more than 0.30 per cent of the alkaloids of belladonna.

Each 100 square centimeters of the spread plaster contains at least 2.5 Gm. of the belladonna plaster mass.

Assay.—See U.S.P., p. 140.

Remarks.—This plaster, for the preparation of the mass of which former Pharmacopœias gave minute directions, is now permitted to be the commercial machine-spread product made with a rubber base. An elaborate assay is provided.

EMPLASTRUM CANTHARIDIS—Cantharides Plaster

(Emp. Canthar.)

Condensed Recipe.

Spread cantharides cerate on a piece of spread adhesive plaster, leaving proper margin. Each square centimeter should contain not less than 0.1 Gm. of the cerate. Permission is given to spread the cerate on muslin or on paper For details see U.S.P., pp. 140 and 141.

Remarks.—This official plaster, the well-known *fly blister*, is cerate of cantharides spread on adhesive plaster. In making it, a piece of the adhesive plaster of the appropriate size is cut off from the roll, the area to be covered inclosed by strips of stiff paper, and the cerate spread by means of a spatula over the exposed portion of the plaster. When spread, the plaster is sometimes finished by sprinkling with a small quantity of vinegar of cantharides or a minute trace of cantharides. Cantharides cerate is the most satisfactory method of producing a blister, and in inflammatory diseases the fly blister is of great value.

It will be noticed that the Pharmacopœia directs that each square centimeter of plaster contain 0.1 Gm. cerate.

EMPLASTRUM SINAPIS—Mustard Plaster

(**Emp. Sinap.**—Mustard Paper)

A uniform mixture of powdered black mustard (deprived of its fixed oil) and a solution of rubber, spread on paper, cotton cloth, or other suitable backing material.

Each 100 square centimeters of spread plaster contains not less than 2.5 Gm. of black mustard deprived of its fixed oil.

When moistened thoroughly with tepid water and applied to the skin, the plaster produces a decided warmth and reddening of the skin within five minutes.

Storage.—Preserve mustard plaster in well-closed containers.

Note.—Before applying mustard plaster it should be thoroughly moistened with tepid water.

Remarks.—In former editions of the Pharmacopœia, this plaster was known as *mustard paper*, the only difference being that in the monograph just given, permission is given to spread the material on cloth, as well as on paper. The plaster is prepared by mixing powdered black mustard (which has been freed from oil by percolation with benzin) with a solution of India rubber in benzin and carbon disulfide, and spreading the semiliquid magma on a piece of stiff well-sized paper (by means of a suitable brush), the Pharmacopœia requiring that 100 square centimeters of such paper should contain not less than 2.5 Gm. of black mustard deprived of oil. The object of first extracting the mustard with benzin is to free it from the fixed oil naturally existing in the seed, and which, if permitted to remain in the mustard paper, would rapidly cause it to become greasy and disagreeable to handle. Mustard paper (*mustard leaves*, as they are called) affords an elegant and convenient method of applying the mustard plaster. When such a mustard leaf is dipped into warm water, a chemical action sets up between the enzyme myrosin and the glucoside potassium myronate, naturally existing in the mixture, with the formation of the volatile oil of mustard. (See p. 754.) The Pharmacopœia directs that the leaf be dipped in warm water, since dipping it in cold water retards the chemical action to a certain extent. On the other hand, it is far preferable to dip into cold water than into hot water, and under no circumstances should the mustard paper be moistened with boiling water, as the heat is sufficient to destroy the delicate enzyme, myrosin, and thus prevent the formation of the volatile oil.

Mustard leaves are applied externally as a rubefacient and local irritant, being particularly adapted for cases of acute indigestion.

Emplastrum Capsici (U.S.P. X) or *Capsicum Plaster* contains not less than 0.25 Gm. of oleoresin of capsicum in each 15 square cm. While former Pharmacopœias gave directions as to painting the oleoresin upon a piece of spread adhesive plaster, the U.S.P. X gave only the rubric printed above. When made extemporaneously, great care should be used in spreading this plaster, the object being to uniformly distribute the oleoresin of capsicum as well as to limit the amount of this irritating substance employed. The oleoresin is chosen in preference to the drug because the latter, blended with the plaster base, would soon lose its activity. For this reason these plasters should be dispensed freshly prepared.

Emplastrum Plumbi Oleatis (U.S.P. X; N.F. VI) or *Lead Plaster*, also called *diachylon plaster* is made from lead monoxide, olive oil, lard, and water as explained in detail on page 609.

Emplastrum Ichthyocollæ (U.S.P., 1890) is made by spreading aqueous solution of isinglass by means of a brush upon taffeta, successive layers of isinglass being applied to this fabric (a variety of silk) until the coating is sufficiently thick. The last portion of isinglass solution is mixed with alcohol and glycerin and applied in the same manner. The back of the taffeta is then spread with tincture of benzoin, and the official plaster allowed to become perfectly dried. Isinglass plaster is the well-known *court-plaster*, and is intended for adhesive purposes in simple operations, such as bringing the two edges of open cuts together. It has no medical action.

Emplastrum Picis Burgundicæ.—This is made by softening Burgundy pitch with yellow wax and olive oil, the Burgundy pitch being so brittle that, if melted and spread on cloth by itself and allowed to become quite cold, the finished plaster will break very quickly. Burgundy pitch plasters formerly enjoyed a large sale under the name of "*poor man's plaster.*"

Emplastrum Resinæ (U.S.P. IX) is made by melting together 800 Gm. lead plaster and 60 Gm. yellow wax, then adding 140 Gm. rosin and when the mixture has liquefied straining it and stirring it until solid. Rosin plaster, when spread constitutes the old-fashioned *sticking plaster.* The spreading is done by means of a special apparatus consisting of reels on one of which the original bolt of cloth is placed; the unrolled cloth passing between the lower plate of stone or metal, and a receptacle containing the melted plaster mass; one side of the receptacle consists of a dull steel blade resting ⅛ or ¼ inch above the slightly stretched cloth. The melted mass trickles upon the cloth in a broad stream, covering the entire width of the cloth, save a small marginal edge. As the soft mass flows upon the cloth it is rapidly passed between the spreading apparatus described above, and emerges from the same with a thin and uniform coating of the plaster material. The rubber adhesive plaster (p. 377) has practically driven this old-fashioned plaster from the market.

LABORATORY EXERCISES

MAKE RESIN PLASTER

Recipe.—		
	Resin, in fine powder	3.5 Gm.
	Lead plaster	20.0 Gm.
	Yellow wax	1.5 Gm.

Melt the lead plaster and yellow wax together with a gentle heat; then add the resin, and, when it is melted, mix the mass thoroughly.

Remarks on Process.—The recipe just given is practically that of U.S.P. IX. Melt the mixture in pint evaporating dish and strain into a tin or tinned-iron dipper.

SPREAD A RESIN PLASTER

The spreading of plasters has become a lost art, but every pharmacist should have sufficient practice to know how to spread one in an emergency.

A plaster is usually spread either on leather (the commercial variety called split skin) or on muslin. This, for convenience, we will call the foundation.

For laboratory practice a sheet of paper can be used. Let the material on which the plaster is spread be sufficiently large to permit a margin of at least an inch all around after the plaster is spread.

The leather, cloth, or paper is carefully stretched over a perfectly level board (the clean counter will do, if it can be pierced with pins), and fastened down at margins with the brass or nickle-headed tacks known commercially as thumb tacks. With paper, this stretching is unnecessary.

Strips of fairly heavy linen paper are cut with an exact, sharp margin, the strips being about 2 inches wide and 8 inches long. The strips are placed on the stretched plaster paper in such a way as to form an exactly even frame inclosing a space the size of the plaster directed to be spread; in this case, 4 by 6 inches. The strips are fastened at each corner by thumb tacks, and when made secure the tacks originally used for stretching the leather—if leather is used—may be removed. (Figs. 254 and 255.)

This done, the plaster mass in tin dipper is cautiously fused, and when melted, small portions of the molten mass are taken out with a spatula and smeared between strips and foundation in very thin layer, in order to fasten the strips to the foundation. Then the spatula is carefully cleaned by passing through a flame of Bunsen burner and wiping off on paper. The foundation should be placed with the length running with the length of the counter, and on this, at narrow end to the left, should be poured the fused mass, so as to cover about one third the length of the plaster. Then, without loss of time, the spatula should be warmed by passing through the flame, and being held in the right hand with blade slightly inclined forward, but perfectly level, about ¼ to ½ inch above the whole width of plaster, the spatula should be moved rapidly and firmly to the right, pushing before it the still molten plaster mass and leaving behind a smooth, shining spread plaster.

Remarks on Process.—The *spatula* should be at least 8 inches long, and should not be sufficiently heated to decompose the plaster mass.

The *plaster mass* should be cautiously fused—not too hot to decompose or to run through the foundation, and yet limpid enough to remain fused until the plaster is entirely spread.

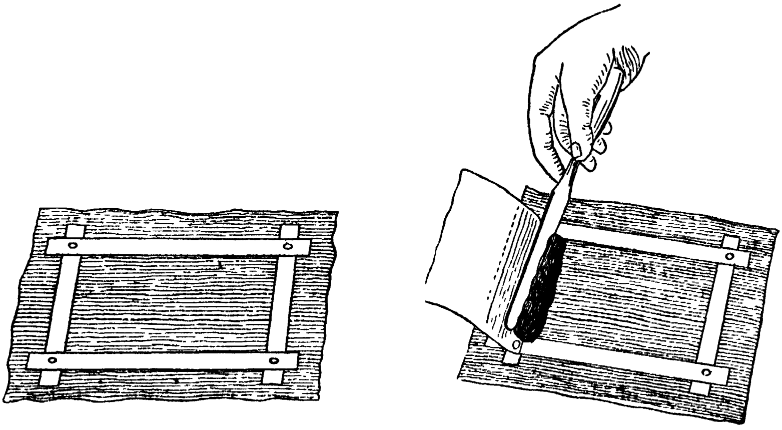
Running the spatula over the fused mass is the delicate part of the process. It must be done as quickly as possible lest the mass solidifies before the process is complete. The spatula must be held perfectly steady else the plaster will be uneven.

In fastening the foundation to the counter place it an inch or so from the edge of the counter, thus leaving a rest for the hand holding the spatula as it passes over the mass.

Remove the strips from the plaster by taking out thumb tacks and pulling off. If the mass is brittle, passing a warm spatula over the strips sometimes aids in loosening them, though this must be done with caution, lest the plaster itself become smeary. The strips removed, a clearly defined plaster should remain, the excess of the mass having been removed with the strips.

The *excess of mass on strips* can be scraped off the strips with warm spatula and left for use another time.

There is little use to attempt to redeem a poorly spread plaster by "reironing"; that is, by trying to smooth it with a warm spatula. The best thing to do is to scrape the mass from the foundation with warm spatula and try over again.



Figs. 254 and 255.—Spreading a plaster.

Other plans for plaster spreading by hand have been followed with more or less success. Thus, for the paper strips, strips of pasteboard ¼ inch thick have been used, and the entire space within the frame filled with the molten mass, the excess being scraped off with the warm spatula. Others cut the frame from an entire sheet of paper.

For *machine spreading of plasters,* see p. 375.

PAPERS

These represent a class of pharmaceuticals in which the medicine is either spread upon paper or absorbed by it. They are not included in the U.S.P. XI or N.F. VI.

Charta Sinapis (U.S.P. VIII) is now included among the plasters (p. 378).

Charta Potassii Nitratis (U.S.P. 1890; N.F. V) is made by dipping white, unsized paper (either filter paper or blotting paper) into a 20 per cent aqueous solution of potassium nitrate, and drying the pieces so dipped. It is intended to be burnt and the vapor inhaled in cases of asthma.

BIBLIOGRAPHY

Cerates.—(Goulard's) Wootton, 1, 1910, 265. (Basilicon) Wootton, 2, 1910, 282.

Ointments.—(Manufacture and uses) Corlett and Hopp, Cleve. Med. Jl., 10, 1911, 202 and 208; Sutton, C.A., 2, 1908, 2707; Stephan, Dr. Circ., 55, 1911, 349; Coppez, C.A., 16, 1922, 3166; Jones, Pract. Dr., 38, Sept., 1919, 36; McNeary, Proc. P.P.A., 43, 1920, 152. (Dispensing) Hodgkin, Ph. Jl., 1, 1841, 207; Beringer, N.J. Ph.A.,

4, 1913, 78; Anon., Ap. Zt., 22, 1907, 1107; Neukam, Ch. Zt., through C.A., 15, 1921, 2150; Jaudon, C.A., 11, 1917, 2717; Holmes, Jl. Phys. Ch., 29, 1925, 1205; Stern, C.A., 21, 1927, 134; Rapp, Ph. Zt., 75, 1930, 303; Gershenfeld and Miller, A.J.P., 105, 1933, 194; Starkman, Canadian Ph. Jl., 66, 1933, 728. (Antiseptic action) Reddish and Wales, Jl. A.Ph.A., 18, 1929, 577; Macht., *ibid.*, 19, 1930, 566. (Iodine) Duhamel, A.J.P., 6, 1834, 116; Zeigler, Jl. A.Ph.A., 17, 1928, 648; LaWall and Tice, Jl. A.Ph.A., 20, 1931, 783. (Stainless iodine) Platt and Smith, Ph. Jl., 95 (1915) 544; Mackie and Sharman, *ibid.*, 113, 1924, 109 and 170. (Cold cream) Durand, A.J.P., 5, 1834, 32 and 77; Turnbull, *ibid.*, 16, 1845, 17; Groat, Jl. A.Ph.A., 4, 1915, 169; Roon, *ibid.*, 6, 1917, 263; Scoville, Jl. A.Ph.A., 19, 1930, 858. (Theatrical cold cream) Alpers, A.Ph.A., 49, 1901, 614. (Diachylon) Vulpius, A.J.P., 50, 1879, 597; Anon., Ch. and Dr., 81, 1912, 906. (Mercurial) Zwick, Jl. A.M.A., 83, 1924, 1821; Ducasse, C.A., 20, 1926, 965; Jordan and Broady, Jl. A.Ph.A., 16, 1927, 425; Franklin, Ph. Jl., 121, 1928, 85; Holdermann, Ph. Zt., 74, 1929, 1097. (Potassium iodide) O.R., Schw. Ap. Zt., 52, 1914, 2921; Taylor Jl A.Ph.A., 11, 1922, 705; Husa, Jl. A.Ph.A., 19, 1930, 825. (Zinc oxide) Sollmann, Jl. A.M.A., 75, 1920, 1420; Clark, Jl. A.Ph.A., 9, 1920, 1171; Hahn and Fischelis, Proc., P.P.A., 44, 1921, 124; Miller, Jl. A.Ph.A., 20, 1931, 779. (Yellow oxide of mercury) Horsford and McKenney, A.J.P., 105, 1933, 251. (Calamine) Raubenheimer, Jl. A.Ph.A., 18, 1929, 270.

Oculenta.—Berry, Ph. Jl., 130, 1933, 64.

Cataplasm of Kaolin.—Stanislaus, A.Ph.A., 56, 1908, 69.

Plasters.—(History) Medberry, West. Dr., 18, 1896, 105; Kilmer, A.J.P., 82, 1910, 416. (Spreading) Bakes, A.Ph.A., 12, 1864, 230; Rice,. Am. Dr., 15, 1886, 106. (Belladonna) Kilmer and Hunt, Jl. A.Ph.A., 14, 1925, 241. (Court plaster) Liston, A.J.P., 13, 1842, 320; Dietrich, Am. Dr., 16, 1887, 66; Rhâne, Ph. Zt., through Ph. Week., 54, 1917, 147. (Diachylon) Peter, Am. Dr., 16, 1887, 22. (Rubber) Edmondson, Proc. P.P.A., 10, 1887, 174; Kilmer, Ph. Era, 68, Apr., 1931, 19; Knoll, Apoth. Zt., 44, 1929, 1255.

Mustard Paper.—Anon., A.J.P., 40, 1868, 276; Anon., Ch. and Dr., 77, 1910, 438.

PART III

INORGANIC CHEMISTRY

CHAPTER XXII

FUNDAMENTALS

A THOROUGH explanation of the sciences of physics and chemistry is beyond the scope of this work, and for complete information on these two sciences the reader is referred to the several works on these subjects noted in the bibliography at the end of this chapter.

There are, however, some facts connected with these two sciences the knowledge of which is essential to a student of the succeeding chapters of this work, and these essential facts are here given.

Matter is anything that has extension (possesses length, breadth, and thickness) or is appreciable to our senses (can be seen, felt, tasted, or smelled). Thus, water is matter, and likewise anything else on this earth or in the air around us, which we can touch, which our senses tell us exists, is matter. All matter is divided into solids, liquids, and gases.

A *solid* is that form of matter which holds a definite shape—whose molecules do not move among themselves.

A *liquid* is that form which is mobile—which assumes the shape of the vessel in which it is placed; whose molecules move freely among themselves.

A *gas* is that form of matter whose molecules tend to separate from one another.

When we call any portion of matter a solid, a liquid, or a gas, we mean that it usually assumes the form which we call it. We know that water, usually a liquid, can be frozen into a solid—ice—or converted by heat into gas—steam. Such is the case with all other matter. Each kind of matter can be changed from the form it usually assumes—be it solid, liquid, or gas—into the other two forms, although sometimes the conversion is very difficult.

Thus, we formerly talked of "permanent gases," by which was meant gases—air, for instance—which could not be converted into liquid or solid form; but not only have the so-called "permanent gases" been turned into liquids, but into solids as well.

The word "molecule," used above, is one of the classes into which we group matter, according as we can divide it or break it up. A piece of coal can be taken and broken up into small pieces. These small pieces can be finely powdered, and by certain means we can divide it still more minutely. According to the extent to which this division is carried on we group matter into masses, molecules, and atoms.

A *mass* is any particle of matter appreciable to our senses. Thus, a big lump of coal or the finest particle of its powder are alike masses.

A *molecule* is the smallest particle of matter that can exist in a free state.

Thus, if we take a dye, dissolve it in water, and keep on diluting the solution, the color grows fainter and fainter until finally we reach a point where the tint almost disappears. It is at a dilution beyond this point where we have the dye divided into its molecules. The eye can observe some very high dilutions; thus, Hoffmann found that one-seven-millionth of a gram of dye in 1 cc. of solution still had a pink tint. Molecules, however, are much smaller than the above illustration would indicate. Van der Waals has calculated that 1 Gm. of hydrogen contains 35×10^{22} molecules, that is, in 1 Gm. there are 350,000,000,000,000,000,000,000 or 350 sextillion molecules, a figure almost beyond the grasp of the intellect.

Finally, we can imagine a subdivision so minute that the dye is separated into the carbon, hydrogen, oxygen, and nitrogen of which it is composed. Then we have reached the atom.

An *atom* is the smallest particle which enters into a chemical combination.

For the modern conception of atoms and molecules, see the end of the chapter.

Physics treats of the *molecular* changes of bodies, while *chemistry* studies the *atomic* changes.

Thus, we heat an iron rod. It turns red and finally softens and glows with white light. But when we allow it to cool, we find it unchanged. In other words, the molecules were temporarily changed. The iron had undergone a *physical change.*

We take powdered iron and powdered sulfur and rub them together, when we get a grayish-yellow powder from which we can separate the iron with magnet or can see its minute particles through a microscope. Intimate though the incorporation may seem, we have merely a mechanical mixture, the molecules of the iron and of the sulfur being absolutely unchanged. We heat this mixture; not merely do the sulfur and the iron molecules undergo the physical change called heating, but the molecules are broken up, the atoms of which they are composed enter into the play, and, through the breaking of the old association and the formation of the new, we get a steel-gray solid, totally different from the iron and the sulfur of which it is composed, from which the iron can no longer be withdrawn by the magnet; in which we can no longer see the particles of iron by means of the microscope. We have a new compound—iron sulfide; for the molecules of iron and sulfur have broken up, their constituent atoms uniting in another combination. Such is a *chemical change.*

We have spoken of carbon, hydrogen, oxygen, nitrogen, sulfur, and iron. What are such kinds of matter? You will notice that we have spoken of *atoms* of these kinds of matter; so you can see that they are capable of very fine division.

Let us think of a mass of sea water. If we attempt to separate it into its constituents, we will find water, salt, magnesium chloride, and many other bodies. Suppose we analyze the salt it contains. This we can divide into sodium and chlorine. Turning our attention to the separated sodium and chlorine: can we break them up as we have the salt or the sea water? Formerly we said "we cannot" and then we added that an *element* is matter that cannot be broken into anything simpler. However some of the research of the past thirty years (outlined at the end of this chapter) raises the question as to whether it would not be better to say "has not, as yet, been broken into anything simpler."

Over eighty elements have been isolated, and of these, less than half are of interest in pharmacy.

A table of those of pharmaceutic importance will be found on p. 390, each accompanied by its symbol, atomic weight, and valence, and grouped in one of the two columns according as it is electropositive or electronegative.

By *symbol* we mean an abbreviation representing the element.

The abbreviation is usually the first letter of the Latin name of the element, but when that letter is already the symbol of an element, then a second letter is added to make the symbol distinctive.

Thus:

	LATIN	SYMBOL
Carbon	Carbo.	C.
Calcium	Calcium.	Ca.
Cerium	Cerium.	Ce.
Cobalt	Cobaltum.	Co.
Copper	Cuprum.	Cu.
Columbium	Columbium.	Cb.
Cadmium	Cadmium.	Cd.
Chlorine	Chlorum.	Cl.
Chromium	Chromium.	Cr.
Cesium	Cæsium.	Cs.

This symbol does not merely mean the element in question in a general way, but when written, indicates the quantity of the element. Thus Ca means one atom of calcium. If we desire to express any other number of atoms, we do so by placing below and to the right of the symbol a small Arabic number representing that quantity.

Thus, while Ca means 1 atom of calcium
Ca_2 means 2 atoms of calcium
Ca_3 means 3 atoms of calcium, etc.

By *symbolic formula* we mean a combination of symbols expressing the composition of a compound molecule. Thus, NaCl means one atom of sodium and one atom of chlorine, making together one molecule of sodium chloride.

H_2SO_4 means two atoms of hydrogen, one atom of sulfur, and four atoms of oxygen, making together one molecule of sulfuric acid.

KNO_3 means one atom of potassium, one atom of nitrogen, and three atoms of oxygen, making together one molecule of potassium nitrate.

ATOMIC WEIGHT

The atomic weight of an element is *the relative combining weight of that element* when compared to hydrogen—the lightest of all substances—as a unit.

Elements combine with each other only in definite proportions. Thus, it has been proved, time and again, that if 63 Gm. of pure copper be heated in a stream of oxygen, 79 Gm. of copper oxide invariably result. This shows that the relative weights when copper and oxygen combine are respectively 63 and 16 ($63 + 16 = 79$).

But how do the combining weights of these elements compare with hydrogen? Copper and hydrogen scarcely unite. Oxygen and hydrogen do; although the estimation of the combining proportions of the two is more complicated than that between copper and oxygen, and an explanation is needed.

It is found that *two* volumes of hydrogen gas (let us say, for example, 2 pints) unite with *one* volume of oxygen gas (say, 1 pint) to form water, and this is still better proved by the fact that water, decomposed by electricity, gives always *two* volumes of hydrogen to *one* of oxygen.

An Italian named Avogadro discovered that equal volumes of different gases contained the same number of molecules. The principle here stated is known as Avogadro's law. Then, if water is composed of 2 volumes of hydrogen and 1 volume of oxygen, and if, further, both hydrogen and oxygen contain 2 atoms in each molecule, as will be shown later, then the formula of water is H_2O and not HO.

Now, water is composed of 2 *volumes* of hydrogen and 1 *volume* of oxygen. By weight, however, it is made from the proportion of 1 Gm. of hydrogen and 8 Gm. of oxygen. By uniting the two statements just made, it will be seen, while we have in water only *half* as many volumes of oxygen as of hydrogen, the weight of that quantity of oxygen is eight times greater than the double volume of hydrogen employed. If half weighs eight times as much, then a whole (equal volume) would weigh sixteen, and we, therefore, see that were hydrogen and oxygen to unite volume for volume the relative combining weights would be 1 to 16. Since hydrogen is the lightest of all known matter, it is given the atomic weight, 1; therefore, we say that the atomic weight of oxygen is 16, and, by the same reasoning, that of copper is 63. By similar experimentation, some of which was exceedingly ingenious and painstaking the atomic weights of all the elements have been established.

Atomic weight is sometimes supposed to represent relative weight of an atom of the element under consideration, but, as it is doubtful whether we have ever obtained a free atom of any element, that definition of atomic weight had better be dropped.

It will be noticed, in the table of elements given on p. 390, that the atomic weights are expressed in round numbers, while the atomic weights given in the Pharmacopœia and other standard works are figures with decimal fractions attached.

Thus, while the table on p. 390 gives the atomic weight of sulfur as 32, the Pharmacopœia gives it as 32.06; while the table gives the atomic weight of potassium as 39, the Pharmacopœia gives it as 39.096; and so in many other cases. There has been controversy as to "exact" atomic weights (the figures showing decimal fractions) and the weights expressed in round numbers; a controversy that is being cleared up by conception of isotopes outlined at the end of this chapter. Suffice it to say that in the table in this book the round numbers are given, first, because the memorization of the fractional numbers is a matter of difficulty—and the table under consideration should be memorized—and, second, the so-called "exact" atomic weights change year by year with the publication of new researches with the combining weights of the elements; moreover, for all the practical purposes of pharmacy, the round number atomic weights are sufficiently exact.

Accepting the "exact" atomic weights, there are three methods of utilizing same:

(*a*) Considering the ratio between hydrogen and oxygen as 1.008 to 16. This basis (O = 16) is the standard that at present is most largely accepted. It is the standard used in the Pharmacopœia.

(*b*) The ratio, H = 1 : O = 15.88. This was the original basis of atomic weights and is in truth the logical one. Partington and also Gray favor the return to this ratio.

(*c*) The Ostwald basis that 22.4 liters of a substance in the gaseous form (compared to hydrogen as standard) weighs the molecular weight of the substance expressed in grams. This figure is not true unless we accept the atomic weight of hydrogen as 1.00.

MOLECULAR WEIGHT

The molecular weight of a substance is the sum of the atomic weights of its constituent atoms. Thus, the molecular weight of sodium chloride (NaCl) is:

Na, atomic weight	23.0
Cl, " "	35.5
NaCl, molecular weight	58.5

The molecular weight of $CaCl_2$ is:

Ca, atomic weight	40	$Ca = 1 \times 40 = 40$
Cl, " "	35.5	$Cl_2 = 2 \times 35.5 = 71$
		$Ca\,Cl_2$ molecular weight, 111

We have means of determining molecular weight that are quite different from the process of finding the atomic weight of elements, and, as the molecular weights of elements found by such processes are almost always twice the atomic weight, we are led to believe that most elemental molecules in the gaseous form contain 2 atoms.

Thus, the molecular weight of oxygen is 32; the atomic weight is 16; therefore a molecule of oxygen must be O_2. On the other hand, while the atomic weight of mercury is 200, its molecular weight estimation gives the same figure, and we are, therefore, forced to the conclusion that a molecule of mercury in the gaseous form consists of 1 atom.

Again, atomic weight estimation of phosphorus shows 31 as its relative combining weight, while its molecular weight has been experimentally proved to be 124; hence 1 molecule of phosphorus in the gaseous form must contain 4 atoms.

VALENCE

Valence is *the relative power which an element* exerts in uniting with or replacing other elements. Thus, analysis of the four typical compounds cited below gives the formula there stated:

Hydrochloric acid	HCl.
Water	H_2O.
Ammonia gas	H_3N (or NH_3).
Methane (marsh gas)	H_4C (or CH_4).

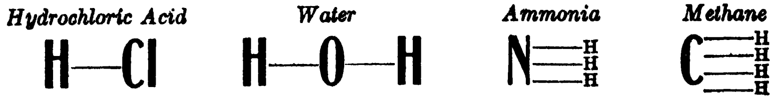
Why is it that while chlorine unites with 1 atom of hydrogen, oxygen can take up 2, nitrogen (N) 3, and carbon (C) 4 atoms of hydrogen? Simply because carbon has four times the combining *power* of hydrogen or chlorine, and twice the combining power of oxygen. Valence has nothing to do with atomic weight. While the latter concerns itself over combining *weight*, valence refers only to combining *power*. That carbon has the valence four—has four times the combining power of hydrogen—is analogous to the fact that a four-dollar check would have four times the purchasing power of a one-dollar check. Akin to this is the illustration that a man with four hands could do four times as much grasping as a man with one hand. This brings up the graphic way of illustrating valence called after its originator, "Frankland's bonds."

Frankland represented valence after this idea of hands, sketching the symbol of the element with as many lines as its valency.

Thus:

Hydrogen	with valence	one	is sketched as	H—
Chlorine	"	one	"	Cl—
Oxygen	"	two	"	O=
Nitrogen	"	three	"	N≡
Carbon	"	four	"	C≣

while the compounds cited above are given the following graphic formula:



To get the idea of valence imagine hydrogen and chlorine as one-armed men clasping hands; oxygen, with two hands going down the street with two single-handed hydrogen atoms; nitrogen as a three-handed being, and carbon as possessing four hands.

It is hardly necessary to state that this picture is purely fanciful; in fact, as outlined at the end of this chapter, we believe that valence is the proportional variation of electric manifestation. The entire theory of valence and especially the varying valences exhibited by the same element is now open to question, but be this as it may, the fact still remains that the theory of valence affords the only rational and practical way of learning to write the symbolic formulæ of chemicals, and in this spirit the subject is discussed in these pages.

In the four compounds given as examples of valence, hydrogen plays a leading part, but when we consider the entire vast mass of chemical compounds we find that the hydrogen compounds are comparatively few, and that oxygen is the element preeminent for combinations. This is well shown in the combinations of chlorine. Hydrogen and chlorine unite to only one compound, the hydrochloric acid (HCl) given above. But when we look up the combinations of chlorine and oxygen, either free or in combination, we find four different bodies having the following formulas.

$$Cl_2O, \quad Cl_2O_3, \quad Cl_2O_5, \quad \text{and } Cl_2O_7.$$

We know that the valence of oxygen is two, that each atom has two bonds: then let us see how the linking power of chlorine varies, by analyzing the four formulas given above.

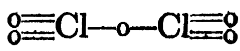
It is evident that the first, Cl_2O, which is analogous to H_2O, has as graphic formula Cl—O—Cl, and that the valence of chlorine is one.

Now for Cl_2O_3. Three atoms of oxygen means six bonds to be divided between two atoms of chlorine. Therefore, each chlorine must take up three bonds of oxygen, giving the graphic formula

$$O=Cl-O-Cl=O$$

In Cl_2O_3 the valence of chlorine must be three.

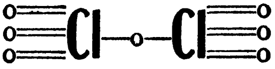
In Cl_2O_5 the five oxygen atoms give us ten bonds, so each chlorine must make up five bonds, thus:



$$\begin{matrix}O=\\O=\end{matrix}Cl-O-Cl\begin{matrix}=O\\=O\end{matrix}$$

and the valence of chlorine is five.

In Cl_2O_7 the seven oxygen atoms mean fourteen bonds, with seven bonds for each chlorine to take up, thus:



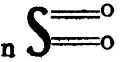
$$\begin{matrix}O=\\O=\\O=\end{matrix}Cl-O-Cl\begin{matrix}=O\\=O\\=O\end{matrix}$$

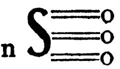
and in this case the valence of chlorine must be seven.

Then, we have three combinations of sulfur, with oxygen:

SO, SO_2, and SO_3.

In $\mathrm{S{=}O}$ the valence of sulfur must be two.

In  $\mathrm{S}\begin{matrix}\mathrm{=O}\\ \mathrm{=O}\end{matrix}$ " " " four.

In  $\mathrm{S}\begin{matrix}\mathrm{=O}\\ \mathrm{=O}\\ \mathrm{=O}\end{matrix}$ " " " six.

The valence of an element is expressed in Roman numerals above and to the right of its symbol; thus, chlorine is expressed as Cl^{I}, Cl^{III}, Cl^{V}, or Cl^{VII} respectively, according as its valence is one, three, five, or seven.

In the table of elements found on the following page not only is the valence and atomic weight of each element given, but the elements are grouped in two columns, according as they are electropositive or electronegative.

These two terms indicate the behavior of the elements when compounds containing them are subjected to the action of a current of electricity.

The subject of electricity is beyond the scope of this work, and here mention can be made only of the fact that electricity is developed by the dynamo, such as can be seen at any electric lighting station, and the electric cell or its combinations into batteries.

From every electric cell two wires emerge, and through these wires pass electricity of different quality, called positive and negative, and the termination of the two wires are called the positive pole and the negative pole respectively.

If we take common salt, sodium chloride, melt it and subject it, while molten, to a current of electricity, at the positive pole of the battery we get the odor of chlorine; while at the negative pole we get metallic sodium.

Now, the electric rule is: "Like electricities repel each other; unlike attract each other," and, since sodium goes to the negative pole, we call it positive; while chlorine, going to the positive pole, is called negative. Accordingly, we see that sodium chloride contains one portion that is positive and another that is negative, and, from this, Berzelius worked out his electromagnetic theory, by which he divided every chemical compound into positive and negative parts, and attempted to explain chemical action by electric influence. But his theory did not stand the test of time, and it has been replaced by the theories as to ions and electrons outlined at the end of this chapter. As just mentioned under electrolytic dissociation, the metals are shown to be positive, while the nonmetallic elements are negative. The division, however, is purely relative. Thus, when zinc is combined with chlorine it is the positive part of the compound; whereas, when combined with sodium it is found in the negative ion.

Chromium (Cr, at. wt. 52) and manganese (Mn, at. wt. 55), while found in official compounds, are omitted from the table for reasons given on pp. 550 and 541.

Following the theory of variation in valence cited on p. 388, it is seen that the variations are usually by two—I, III, V, VII or II, IV, VI—mercury, iron, and copper being the only exceptions in the table on p. 390. The irregular variations of these will be explained later.

ELEMENTAL TABLE

	NEGATIVE −			POSITIVE +		
	Name	*Symbol and valence*	*Atomic weight*	*Name*	*Symbol and valence*	*Atomic weight*
MONADS. (Usually having valence I.)	Chlorine	Cl. I III V VII	35.5	Lithium	Li. I	7
	Bromine	Br. I III V VII	80.0	Sodium	Na. I	23
	Iodine	I. I III V VII	127.0	Potassium	K. I	39
				Copper (“ous” form)	Cu. I	63
				Silver	Ag. I	108
				Mercury (“ous” form)	Hg. I	200
DYADS. (Usually having two bonds—the valence II.)	Oxygen	O. II	16.0	Magnesium	Mg. II	24
	Sulfur	S. II IV VI	32.0	Calcium	Ca II	40
				Strontium	Sr. II	88
				Barium	Ba. II	137
				Iron (“ous” form)	Fe II	56
				Copper (“ic” form)	Cu. II	63
				Zinc	Zinc II	65
				Mercury (“ic” form)	Hg II	200
				Lead	Pb. II	207
				Tin (“ous” form)	Sn. II	119
TRIADS. (Having the valence III, usually.)	Boron	B. III	11.0	Aluminum	Al. III	27
	Nitrogen	N. III V	14.0	Iron (“ic” form)	Fe. III	56
	Phosphorus	P. III V	31.0	Gold	Au. III	197
	Arsenic	As III V	75.0	Bismuth	Bi. III	209
	Antimony	Sb. III V	120.0	Cerium	Ce. III	140
TETRADS. (Valence of IV.)	Carbon	C. IV	12.0	Tin (“ic”) form)	Sn. IV	119
	Silicon	Si. IV	28.0			

Having considered the subject of chemistry from the standpoint of the individual elements, we can now take up the subject, grouping of elements, thus entering into the domain of chemical compounds.

COMPOUNDS

We have spoken of molecules as the smallest particles of matter existing in a free state, and we mentioned among others the molecule of oxygen. Such an elemental molecule is called a *simple* molecule, in distinction to *compound* molecules; those containing at least two different kinds of elements. Thus, while O_2, S_2, or P_4 are examples of simple molecules, NaCl, K_2SO_4, and $KNaC_4H_4O_6$ are types of compound molecules; and while the simple molecules contain only a small number of atoms—usually two—the number of atoms in a compound molecule are practically unlimited; one complex organic body, hemoglobin, containing somewhere around 5000 atoms to the molecule, it is claimed.

Taking up the inorganic compound molecules, we first divide them into two classes—the binary and the ternary compounds.

Binary compounds are those containing two different kinds of elements. Thus, NaCl, KBr, CaO, and Cl_2O_3 are examples of binary compounds.

The naming of binary compounds is simple. We give the name of the positive element first; then the name of the negative element, changing its termination to “ide.” Making this clear by illustration, we will take NaCl as the first example. This consists of sodium and chlorine. The table given above shows that sodium is the positive element and chlorine the negative element of that compound. Accordingly, we call the body sodium chlor*ide*. Remember that the termination “ide” is characteristic of binary compounds.

In writing binary compounds we place the symbol of the positive element first; then the symbol of the negative element, placing below and to the right of each symbol, in Arabic numerals, the respective number of atoms entering into the molecule. Thus $CaCl_2$ means 1 atom of calcium and 2 atoms of chlorine, making a molecule of calcium chloride.

Before leaving binary compounds, mention must be made of the four acids belonging to this group. These four are HCl (hydrochloric acid); HBr (hydrobromic acid); HI (hydriodic acid); and HF (hydrofluoric acid); and they are called the halogen or haloid acids. As acids will come in for discussion in Chapter XXIV, these halogen acids will be left for that time. They must be noted here, however, if for no other reason than as exceptions to the nomenclature—to the naming—of binary compounds.

Ternary compounds are those inorganic bodies containing three or more different kinds of elements. The word "ternary," coming from a Latin root meaning "three," would seem to exclude any compounds other than those containing three kinds of elements. However, as there are comparatively few definite inorganic compounds containing more than three different elements, these few are usually included and discussed with the ternary compounds. The naming of ternary compounds is a matter of some complexity, and before discussing this phase of the question it is necessary to explain the formation of ternary compounds.

All ternary compounds are derived indirectly from binary compounds, the oxides, and it is therefore necessary to discuss these important bodies. If we take the various oxides and combine them with water, we get, according as the distinctive element is positive or negative, an acid or a base, as shown by the two following equations:

$$\begin{aligned}\text{Thus, } P_2O_5 + H_2O &= H_2P_2O_6 = 2HPO_3.\\ CaO + H_2O &= CaO_2H_2 = Ca(OH)_2.\end{aligned}$$

By the term "equation," given above, we mean the representation of a chemical reaction by means of symbolic formulas.

Thus, the first of the two equations given above means that 1 molecule of phosphoric oxide (P_2O_5) combines with 1 molecule of water (H_2O) to make 2 molecules of metaphosphoric acid ($2HPO_3$).

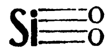
The second means that 1 molecule of calcium oxide (CaO) combines with 1 molecule of water (H_2O) to make 1 molecule of the base, calcium hydroxide ($Ca(OH)_2$).

Details of the writing and the balancing of such equations will be given later (p. 400).

In discussing this matter we will consider, first, the acids and then the bases.

Formation of the Acid Formula.—Going back to the table on p. 390, running down the line of negative elements we find silicon with the valence four.

One atom of silicon with valence four can take up 2 atoms of oxygen with valence two, as shown in the following graphic formula:



or SiO_2.

This body is called silicon oxide or silicic oxide. If this oxide combined with water we would get:

$$\begin{array}{l} SiO_2 \\ H_2\ O \\ \hline H_2SiO_3 \end{array} \quad \text{Silicic Acid.}$$

In another form, $SiO_2 + H_2O = H_2SiO_3$.

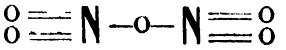
SiO_2 is sand which is insoluble in water; hence the reaction just described does not occur. On the other hand silicic acid upon strong heating gives off water as shown in the following equation:

$$H_2SiO_3 - H_2O = SiO_2$$

It will be noticed that in this oxide and the derived acid the word silicon is changed to sili*cic*.

Suppose we consider the two oxides of nitrogen which combine with water. Looking at the table on p. 390, we find the valence of nitrogen three and five; therefore the oxides must be

$O{=}N{-}O{-}N{=}O$ or N_2O_3 and



$\begin{matrix}O\\O\end{matrix}{=}N{-}O{-}N{=}\begin{matrix}O\\O\end{matrix}$ or N_2O_5

The linkage of the nitrogen and of the oxygen in these 2 cases occurs in a manner precisely the same as the linkage between oxygen and chlorine of valence three and five, as shown on p. 388. In naming these two oxides of nitrogen both cannot be nitr*ic* oxide, so we apply that name to the one in which nitrogen shows the highest valence, calling the other, the one in which nitrogen shows the valence three, nitr*ous* oxide.

Adding water to these, we get the corresponding acids: thus—

(*a*) N_2O_3 (nitr*ous* oxide) $+ H_2O = H_2N_2O_4 = 2HNO_2$ (nitr*ous* acid).
(*b*) N_2O_5 (nitr*ic* oxide) $+ H_2O = H_2N_2O_6 = 2HNO_3$ (nitr*ic* acid).

These two equations can be expressed in words as follows:

(*a*) One molecule of nitrous oxide plus 1 molecule of water gives 2 molecules of nitrous acid.

(*b*) One molecule of nitric oxide plus 1 molecule of water gives 2 molecules of nitric acid.

Unfortunately in customary chemical nomenclature the words nitrous oxide and nitric oxide are applied to other oxides of nitrogen (p. 432). These facts, however, in no way affect the validity of the statements given in the foregoing paragraph.

In other words, with these oxides of nitrogen the molecule of the oxide does not blend with the molecule of water to make 1 molecule of the acid, as was the case in the formula of silicic acid, but *2* molecules result from the combination.

As the symbolic formula expresses the contents of a molecule, the formula of nitrous acid is HNO_2 and the formula of nitric acid is HNO_3.

Looking up sulfur, we find it has three valences, and, therefore, yields three oxides, SO, SO_2, and SO_3. SO_3 we call sulfuric oxide; SO_2, sulfur*ous* oxide; and SO we call *hypo*sulfur*ous* oxide, the prefix "hypo" meaning "under."

Let us see how these three oxides form acids.

SO (*hypo*sulfur*ous* oxide) $+ H_2O = H_2SO_2$ (*hypo*sulfur*ous* acid).
SO_2 (sulfur*ous* oxide) $+ H_2O = H_2SO_3$ (sulfur*ous* acid).
SO_3 (sulfur*ic* oxide) $+ H_2O = H_2SO_4$ (sulfur*ic* acid).

So when we have three acids from one negative element, the name of the negative element in which that element acts with the highest valence is given the termination "*ic*"; the termination in the one in which the element acts with the next lower valence is "*ous*"; while the one in which the element acts with the lowest valence is given the prefix "*hypo*" and the termination "*ous.*"

As noted on p. 388, four oxides of chlorine yielding acids are known: Cl_2O, Cl_2O_3, Cl_2O_5, and Cl_2O_7. In naming these, the one with the lowest valence of chlorine is called "*hypo*chlor*ous*"; the next, "chlor*ous*"; and the next, "chlor*ic*," just as in the preceding. This leaves the fourth to be named, and it is given the prefix "*per*" and the termination "*ic*"—"*per*chlor*ic*." These four oxides yield four acids, as follows:

Cl_2O (*hypo*chlor*ous* oxide) $+ H_2O = H_2Cl_2O_2 = 2HClO$ (*hypo*chlor*ous* acid).
Cl_2O_3 (chlor*ous* oxide) $+ H_2O = H_2Cl_2O_4 = 2HClO_2$ (chlor*ous* acid).
Cl_2O_5 (chlor*ic* oxide) $+ H_2O = H_2Cl_2O_6 = 2HClO_3$ (chlor*ic* acid).
Cl_2O_7 (*per*chlor*ic* oxide) $+ H_2O = H_2Cl_2O_8 = 2HClO_4$ (*per*chlor*ic* acid).

This completes the theoretic formation and naming of acids; the summary of nomenclature being:

If there is one oxyacid from an element it has the termination "*ic*."
If there are two, the higher in valence is "*ic*."
the lower in valence is "*ous*."
If there are three, the highest in valence is "*ic*."
the middle in valence is "*ous*."
the lowest in valence is "*hypo*—*ous*."
If there are four, the lowest in valence is "*hypo*—*ous*."
the next higher in valence is "*ous*."
the next higher in valence is "*ic*."
the highest in valence is "*per*—*ic*."

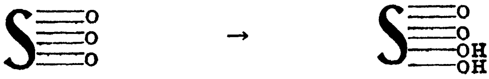
Remember, this method of nomenclature applies only to oxyacids—those acids which contain oxygen.

The four haloid acids have their specific names—hydrochloric, hydrobromic, etc., and do not enter into this category. Do not confuse *hydrochloric* with *chloric* acid. Hydrochloric acid is a binary compound, HCl, while chloric acid is ternary—an oxyacid—$HClO_3$.

It may be well to emphasize that the above explanation of the formation of acids is given merely with the view of teaching the student the writing of formulas, and it is necessary to warn the reader against assuming the conclusion that the practical manufacture of the chemicals whose formulas are thus worked out of necessity follows the same line here suggested. While it is true that sulfuric acid is made by treating sulfuric oxide with water, silicic acid cannot be formed by direct combination of silicic oxide (sand) and water. Again, it might be mentioned that frequently some of the compounds spoken of familiarly when discussing formula writing may be too unstable to exist. This is true of several oxides of chlorine and of iodine.

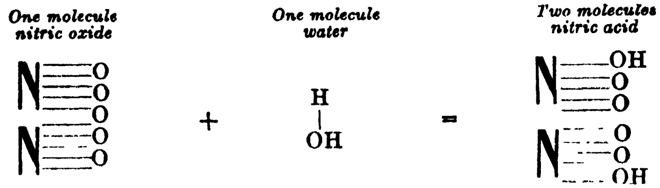
In working out the theoretic formation of the acids given above, the graphic formula of the oxide has been given, followed by the mere statement that the acid is formed by adding water to the oxide. The question that might arise is, How is it possible to add a molecule of water to a saturated compound? In the group SO_3 each of the six bonds of the sulfur are taken up by oxygen, so where can the 2 atoms of hydrogen and 1 of oxygen be attached?

The answer is very simple, for when water (H_2O) is brought in contact with sulfuric oxide (SO_3), the latter arranges with the water to the new groupings here shown:

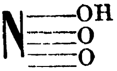


the water breaking into H and OH; one of the O atoms of SO_3 breaking loose from the double union with sulfur and uniting with the free H from the water (forming OH), while the OH group from the water attaches itself to the free sulfur bond, and we get the compound $SO_2(OH)_2$ or H_2SO_4, sulfuric acid, containing two hydroxyls (the radical mentioned on p. 636).

It might be interesting to express graphically the transition of 1 molecule of nitric oxide into 2 molecules of nitric acid, as described above.



It will be seen from this that the graphic formula of nitric acid is



that is, to the atom of nitrogen there are attached 2 atoms of oxygen and one hydroxyl group.

Formation of the Formulas of Bases.—Bases, with the exception of ammonia and its organic derivatives, which we will discuss in due course of time, represent the oxygen and hydrogen compounds of a positive element, and can be derived in exactly the same way as the acids have been from the negative elements—by adding water to the oxides; only in the case of bases the process is much simpler.

In glancing over the positive elements on p. 390, it will be noticed that all these elements, save mercury, iron, and copper, usually exhibit but one valence, and, accordingly, each element usually yields but one base. The nomenclature is much simplified by this fact, bases being named by placing the name of the characteristic element first, followed by the word "hydroxide."

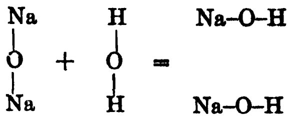
Let us summarize by a few general examples:

Na_2O (sodium oxide) $+ H_2O = Na_2O_2H_2 = 2NaOH$ (sodium hydroxide).
CaO (calcium oxide) $+ H_2O = CaO_2H_2 = Ca(OH)_2$ (calcium hydroxide).
Fe_2O_3 (ferric oxide) $+ 3H_2O = Fe_2O_6H_6 = 2Fe(OH)_3$ (ferric hydroxide).

In the above equations the final formula, whenever possible, has been reduced to its simplest form. Thus, $Na_2O_2H_2$, like $H_2N_2O_4$ of p. 392 can be divided by two, and in truth the molecule of sodium hydroxide is $NaOH$ and not $Na_2O_2H_2$. Again, note that a large figure placed at the commencement of a formula multiplies every element following it by that number; thus $2NaOH$ means $Na_2O_2H_2$; $2HNO_2$ is the same as $H_2N_2O_4$ ($O_2 \times 2$ equals O_4).

It will be seen in the case of calcium hydroxide that CaO_2H_2, containing as it does but 1 atom of calcium, constitutes 1 molecule. In such cases, however, it is considered neater to inclose the oxygen and hydrogen in brackets, with the number of atoms outside the brackets. Thus, CaO_2H_2 is usually expressed as $Ca(OH)_2$. A small figure outside the brackets multiplies each element within the brackets, even as a large figure in front of the formula multiplies every element following it.

Graphically, these hydroxides may be expressed with equal ease as hydroxyl derivatives, each bond of metal taking one OH group, thus:



$$\begin{array}{c} Na \\ | \\ O \\ | \\ Na \end{array} + \begin{array}{c} H \\ | \\ O \\ | \\ H \end{array} = \begin{array}{c} Na\text{–}O\text{–}H \\ \\ Na\text{–}O\text{–}H \end{array}$$

It is customary to make a slight difference in the writing of acids and bases. In writing acids, we place the hydrogen atoms first, then the characteristic element, and finally the oxygen atoms. In bases, on the contrary, the characteristic element comes first, followed by the hydroxyl groups. This is a mere matter of form, the only reason why the two classes of bodies are so differentiated being because it affords a convenient method of distinguishing acid and basic formulas.

It is wise, however, not to get bound down to rigid rules. Different books have different ways of writing formulas; for instance, sulfuric acid can be written $SO_2(OH)_2$ as well as H_2SO_4.

Considerable mention has been made on preceding pages of acids and bases without giving any idea what these bodies really are. The theoretic consideration of them just given is very important, but it does not necessarily represent real practical conditions. Acids and bases had first to be known before theories regarding them were evolved, and it is of greatest importance that they should be known when met with.

The following preliminary definitions should be carefully studied:

An *acid* is a substance which contains hydrogen, turns *blue* litmus paper *red* and combines with bases to form salts.

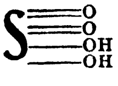
A *base* is a substance which turns *red* litmus paper *blue* and combines with acids to form salts. And, finally,

A *salt* is the product of the combination of an acid and a base.

Litmus paper is an article of commerce made by dipping porous paper in a decoction of litmus, a sort of lichen. A drop of acid (always to be applied in diluted form) will make a red spot on blue litmus paper, and likewise a drop of diluted alkali (as bases are called) will make a blue spot on red litmus paper.

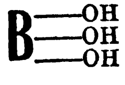
Electrolytic conception of acids, bases and salts will be explained at the end of this chapter.

The three classes, acids, bases, and salts, cover the entire domain of ternary compounds. Before speaking of salts, mention must be made of another point concerning acids. We have just seen that sulfuric acid may be written—



$$S\begin{array}{l} =O \\ =O \\ -OH \\ -OH \end{array}$$

In other words, as a sulfur atom with 2 oxygen atoms and 2 hydroxyl groups attached. If we look up the formula of boric acid, we find it to be H_3BO_3 or, graphically,



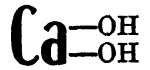
$$B\begin{array}{l} -OH \\ -OH \\ -OH \end{array}$$

In this, each bond of the characteristic atom is taken up by a hydroxyl, and such an acid is called an "ortho" acid. Almost all bases are "ortho," having as many hydroxyls as bonds of the characteristic element, and thus we find—

Sodium hydroxide

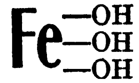
$Na{-}OH$

Calcium hydroxide



$$\mathrm{Ca}\begin{matrix}-OH\\-OH\end{matrix}$$

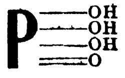
Ferric hydroxide



$$\mathrm{Fe}\begin{matrix}-OH\\-OH\\-OH\end{matrix}$$

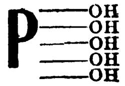
but with acids it is different, and of the oxyacids, *boric acid* is the only official ortho acid.

There is an official acid called orthophosphoric acid (H_3PO_4), but it is not a true ortho-acid in the sense expressed above. Its graphic formula is—



$$\mathrm{P}\begin{matrix}-OH\\-OH\\-OH\\=O\end{matrix}$$

while true ortho-phosphoric acid should be



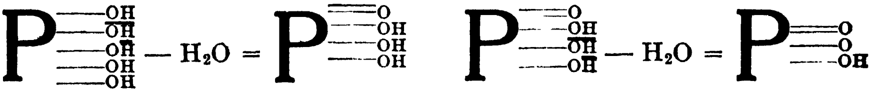
$$\mathrm{P}\begin{matrix}-OH\\-OH\\-OH\\-OH\\-OH\end{matrix}$$

Acids not having all the bonds of the characteristic element taken up by hydroxyl groups are called *meta*-acids, and, accordingly, H_3PO_4 should be classed among the meta-acids.

The original idea of ortho- and meta- combinations was that when two kinds of salts of the same acid were known, the one containing the most metal was called the ortho-salt, while the other was called the meta-salt. Thus, the sodium salt of H_3PO_4 was called orthophosphate of soda, while the sodium salt of HPO_3 was called metaphosphate of soda.

The difference between the three phosphoric acids, H_5PO_5, H_3PO_4, and HPO_3, is simply a loss of water.

It appears that usually the characteristic element cannot carry many hydroxyl groups, and these are parted with by the throwing off of water, as represented in the following graphic sketch.



$$\mathrm{P}\begin{matrix}-OH\\-\overline{OH}\\-O\overline{H}\\-OH\\-OH\end{matrix} - H_2O = \mathrm{P}\begin{matrix}=O\\-OH\\-OH\\-OH\end{matrix} \qquad \mathrm{P}\begin{matrix}=O\\-OH\\-\overline{OH}\\-O\overline{H}\end{matrix} - H_2O = \mathrm{P}\begin{matrix}=O\\=O\\-OH\end{matrix}$$

H_5PO_5 H_3PO_4 H_3PO_4 HPO_3

SALTS

Salts are solids, neutral to test paper, affecting neither the red nor the blue of litmus. Of course, there are exceptions; but this much can be usually stated regarding them. As to the naming of a salt, we place first the name of the metal (the base; the positive element), then the name of the acid, the termination of which is changed to "ate," if we are dealing with an "ic" acid; and to "ite," if it comes from an "ous" acid. This is shown clearly in the names of the oxyacids of chlorine.

Hypochlor*ous* acid gives hypochlor*ites.*

Chlor*ous* acid gives chlor*ites.*

Chlor*ic* acid gives chlor*ates.*

Perchlor*ic* acid gives perchlor*ates.*

The salts of the halogen acids do not come under this method of nomenclature. Such salts are binary compounds, and are given the termination "ide"; thus, hydrochloric acid yields chlorides, hydrobromic acid yields bromides, hydriodic acid yields iodides. The alkaloidal salts of these acids, are, however, called hydrochlorides, hydrobromides, and hydriodides.

The formation of salts is governed by valence, just as is the origin of all other compounds, and to write the formulas of salts intelligently it is essential to know the valence expressed in the table on p. 390.

We have given as the definition of valence "the relative combining power of elements." Valence, however, means more than this, and when we say that the valence of sodium is one, we not only mean that an atom of it can combine with 1 atom of chlorine to form a molecule of sodium chloride, but also (what is the same thing expressed differently) 1 atom of it can *replace* 1 atom of hydrogen in hydrochloric acid (HCl) to form the molecule of sodium chloride. So valence not only means relative combining power, but also the relative power or a metal to replace the hydrogen of an acid.

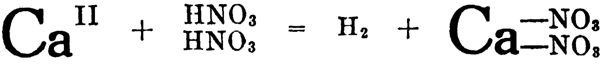
A few examples may perhaps better explain this.

Let us take sodium, with the valence one. One atom can replace 1 atom of hydrogen in an acid.

Nitric acid, HNO_3, has 1 atom of hydrogen; this can be replaced by an atom of sodium, when we get $NaNO_3$, sodium nitrate. Sulfuric acid, H_2SO_4, has 2 atoms of replaceable hydrogen; therefore, 2 atoms of sodium are needed, when we get Na_2SO_4, sodium sulfate.

Now for the combinations of *calcium*, valence two, which means that 1 atom of calcium can replace 2 atoms of hydrogen in an acid.

Nitric acid, HNO_3, has 1 atom of hydrogen; calcium requires two; accordingly, we take 1 atom of calcium and 2 molecules HNO_3, thus:

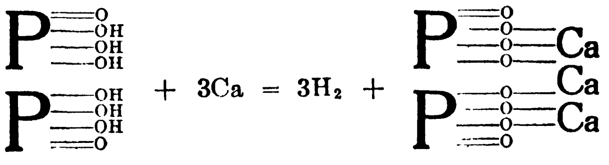


$$\mathrm{Ca}^{\mathrm{II}} + \begin{matrix}\mathrm{HNO_3}\\ \mathrm{HNO_3}\end{matrix} = \mathrm{H_2} + \mathrm{Ca}\begin{matrix}\mathrm{-NO_3}\\ \mathrm{-NO_3}\end{matrix}$$

replacing the 2 hydrogen atoms by one Ca, forming $Ca(NO_3)_2$, calcium nitrate.[1]

Sulfuric acid, H_2SO_4, has 2 atoms of hydrogen. These can be replaced by 1 atom of calcium, when we get $CaSO_4$, calcium sulfate.

Phosphoric acid, H_3PO_4, has three replaceable atoms of hydrogen; calcium requires two. This complicates matters and we had better write the equation graphically:

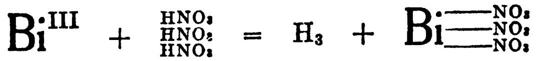


$Ca_3(PO_4)_2$
Calcium phosphate.

the reaction occurring between 3 atoms of calcium and 2 molecules of phosphoric acid, the 6 hydrogen atoms of which are replaced by the 3 calcium atoms.

As the last example, let us take bismuth, valence three; 1 atom of bismuth being able to replace 3 atoms of hydrogen in an acid.

Nitric acid, HNO_3, has one hydrogen; so to combine with bismuth 3 molecules of nitric acid are necessary, thus:



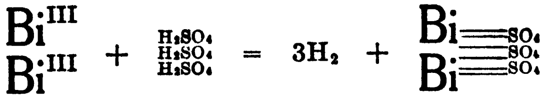
$$\mathrm{Bi}^{\mathrm{III}} + \begin{matrix}\mathrm{HNO_3}\\ \mathrm{HNO_3}\\ \mathrm{HNO_3}\end{matrix} = \mathrm{H_3} + \mathrm{Bi}\begin{matrix}\mathrm{-NO_3}\\ \mathrm{-NO_3}\\ \mathrm{-NO_3}\end{matrix}$$

$Bi(NO_3)_3$
Bismuth nitrate.

---

[1] In this and other replacing equations found in this chapter, the liberation of hydrogen need not be taken too literally. Metallic calcium plus the appropriate acid may liberate hydrogen, but the reaction is too violent to be practical. In general manufacturing the oxide or carbonate of the first and second group of metals is usually employed.

Sulfuric acid, H_2SO_4, has 2 atoms of hydrogen; bismuth requires three; therefore combination occurs between 3 molecules of the acid and 2 atoms of bismuth, thus:



$$\begin{matrix}Bi^{\cdot III}\\ Bi^{\cdot III}\end{matrix} + \begin{matrix}H_2SO_4\\ H_2SO_4\\ H_2SO_4\end{matrix} = 3H_2 + \begin{matrix}Bi\!\!=\!\!SO_4\\ \quad\;\; SO_4\\ Bi\!\!=\!\!SO_4\end{matrix}$$

$Bi_2(SO_4)_3$
Bismuth sulfate.

Phosphoric acid, H_3PO_4, has 3 atoms of hydrogen; bismuth requires three, so the combination should be:

$$Bi + H_3PO_4 = H_3 + BiPO_4$$ Bismuth phosphate.

To sum up the important study of the writing of formulas of salts:

Halogen Salts.—These follow the general rule for binary compounds. Remember that all official compounds the name of whose negative element ends in "ide" are binary, and then follow the general rule for binary formulas given on p. 390; the process being merely a matter of relative valence. As to writing binary compounds, look up the valence of the positive and negative elements of the compounds, and combine these in just such proportions that each will furnish the same number of bonds; viz.:

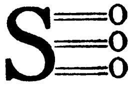
Valences similar,	the elemental union	is	atom for atom.
Valences II and III,	"	"	3 atoms of II to 2 atoms of III.
Valences II and IV,	"	"	2 atoms of II to 1 atom of IV.
Valences II and V,	"	"	5 atoms of II to 2 atoms of V.
Valences II and VI,	"	"	3 atoms of II to 1 atom of VI.
Valences II and VII,	"	"	7 atoms of II to 2 atoms of VII.

Combinations of the valence I with the valence II and VII are so simple that they need not be given. Until the student becomes expert, it is better to work out formulas by the graphic means described on p. 399.

In writing out the empirical formulas of the binary compounds, remember that the symbol of the positive element comes first, then that of the negative, with the number of atoms of each below and to the right of the respective symbols.

Ternary Salts.—In writing a formula of a ternary salt, we first must know the formula of the acid from which it is derived, and this is worked out from the formula of the oxide, which in turn is figured by valence—by the regular rule for the writing of binary formulas. An example can best illustrate this.

We want to know the formula of sodium sulfate and do not know either the formula of sulfuric acid nor of sulfuric oxide. Referring to table of elements on p. 390, we find the valence of sulfur is II, IV, and VI. We are working on sulfuric compounds, and the valence of sulfur in these is its highest, VI, and, graphically, we sketch the oxide.



$$S\begin{matrix}=O\\ =O\\ =O\end{matrix}$$

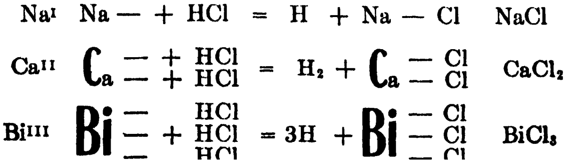
SO_3
Sulfuric oxide.

To make this into sulfuric acid, water is added, by the following reaction:

$$SO_3 + H_2O = H_2SO_4.$$

Thus, learning that the formula of sulfuric acid is H_2SO_4, and remembering that each atom of hydrogen removed from the acid in making a salt calls for one bond of the replacing metal, we now look at the *replacing* *capacity*—the valence—of the metal. We find that sodium has the valence one—that 1 atom of it can replace but 1 atom of hydrogen in an acid. As sulfuric acid has 2 atoms of hydrogen, to replace these, 2 atoms of sodium will be needed, and by this reasoning we learn that the formula of sodium sulfate is Na_2SO_4. All this was fully explained on p. 398.

If deemed preferable, the haloid salts—the salts of hydrochloric, hydrobromic, hydriodic, and hydrofluoric acids—may be worked out by this idea of replacement of hydrogen in an acid by a metal, as the following sketching of the formulas of chlorides will show:

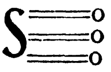


$$\mathrm{Na^{I}}\quad \mathrm{Na}- + \mathrm{HCl} = \mathrm{H} + \mathrm{Na}-\mathrm{Cl}\quad \mathrm{NaCl}$$

$$\mathrm{Ca^{II}}\quad \mathrm{Ca}\begin{array}{l}- + \mathrm{HCl}\\ - + \mathrm{HCl}\end{array} = \mathrm{H_2} + \mathrm{Ca}\begin{array}{l}-\mathrm{Cl}\\ -\mathrm{Cl}\end{array}\quad \mathrm{CaCl_2}$$

$$\mathrm{Bi^{III}}\quad \mathrm{Bi}\begin{array}{l}-\\ -\\ -\end{array} + \begin{array}{l}\mathrm{HCl}\\ \mathrm{HCl}\\ \mathrm{HCl}\end{array} = 3\mathrm{H} + \mathrm{Bi}\begin{array}{l}-\mathrm{Cl}\\ -\mathrm{Cl}\\ -\mathrm{Cl}\end{array}\quad \mathrm{BiCl_3}$$

This explanation can be condensed into the following table of formula writing. If we want the formula of a ternary salt—say sodium sulfate—it can be worked out by answering the following questions:

Question	Answer Applied to the type, sodium sulfate.
1. Of what acid is the compound a salt?	A sulf*ate* is a salt of sulfur*ic* acid, "ic" acids giving "ate" salts.
2. From what oxide is this acid derived?	From sulfur*ic* oxide, the name of the oxide being always that of the acid.
3. What is the characteristic element in this oxide?	Sulfuric acid must come from the element sulfur.
4. What is the valence of this element?	II, IV, and VI, as shown on p. 390.
5. What is the valence of this element in the oxide above mentioned?	"ic" oxide means that oxide showing the highest valence of the element, when the element has three or less valences. Hence in sulfuric oxide sulfur must have the valence VI.
6. What is the graphic formula of this oxide?	One atom of sulfur with valence VI takes three atoms of oxygen (valence II) for saturation, thus:  = SO_3.
7. How is the acid derived from this oxide?	By addition of water, thus, $SO_3 + H_2O = H_2SO_4$.
8. What, then, is the formula of the acid?	H_2SO_4.
9. What is the valence of the metal in the salt?	The table on p. 390 says sodium has the valence I.
10. What does this mean?	That one atom of sodium can replace one atom of hydrogen in an acid.
11. How many atoms of replaceable hydrogen are there in the acid in question?	In H_2SO_4 there are two atoms of replaceable hydrogen.
12. Then how many atoms of the metal are needed to make a molecule of the salt in question?	The two atoms of hydrogen in H_2SO_4, need two atoms of sodium to replace them.
13. What, then, will be the formula of the salt?	Its formula will be Na_2SO_4.

By such reasoning, with the aid of the table on p. 390, practically every formula of a ternary salt can be worked out.

The salts produced as just described—by replacing all the hydrogen of an acid by a metal—are called *normal salts.*

Thus, when the 2 atoms of hydrogen in sulfuric acid (H_2SO_4) are replaced by 2 atoms of sodium, we obtain Na_2SO_4—normal sodium sulfate.

It is possible, however, to replace only 1 atom of hydrogen in the above acid by 1 atom of a monad metal, and if sodium is the metal, we obtain $NaHSO_4$ (sodium bisulfate), 1 hydrogen still remaining in the compound. This atom of hydrogen still exerts its acid properties, and such salts usually turn blue litmus red, and are, therefore, called *acid salts.* Why these salts are given the prefix "bi," as *bi*sulfate, *bi*tartrates, etc., will be explained later.

On treating these *acid salts,* such as potassium bitartrate ($KHC_4H_4O_6$), with the hydroxide or carbonate of another metal (and be it here said that in practice the metal itself is rarely used in making these salts, in many cases it being too dangerous a procedure), the other metal replaces the remaining atom of replaceable hydrogen, thereby forming a *double salt.*

Thus, replacing the hydrogen of $KHC_4H_4O_6$ by an atom of sodium, we obtain potassium and sodium tartrate ($KNaC_4H_4O_6$), or Rochelle salt.

In due course of time (p. 638) it will be explained why only part of the hydrogen of an organic acid is replaceable by a metal.

Besides the normal, acid, and double salts just mentioned, there is a class of salts called *basic salts.* In the acid salts there is predominance of the acid portion; in the basic salts there is a deficiency of such. These basic salts will be more thoroughly considered later. (See p. 570.) So here suffice it to state that most of the "sub" preparations, as bismuth *sub*nitrate, iron *sub*sulfate, etc., are basic salts.

CHEMICAL ARITHMETIC

The pharmaceutic applications of atomic and molecular weights described on pp. 386 and 387 are manifold.

Thus, through molecular weights we are able to *estimate the amount of water of crystallization* in a chemical (p. 172).

For instance, let us figure out the percentage of water of crystallization in the formerly official dekahydrated sodium carbonate.

The formula of this body is $Na_2CO_3.10H_2O$, which means a molecular weight of 286 as the following reckoning will show:

Atomic weight of Na is 23 $Na_2 = 2 \times 23 = 46$
Atomic weight of C " 12 $C = 1 \times 12 = 12$
Atomic weight of O " 16 $O_3 = 3 \times 16 = 48$
Atomic weight of H " 1 $10H_2 = 20 \times 1 = 20$
Atomic weight of O " 16 $10O = 10 \times 16 = 160$
286

The molecular weight of $Na_2CO_310H_2O$ is 286, and of this, 180 parts (20 + 160) represent the 10 molecules of water of crystallization. What percentage of 286 is 180?

This is easily $^{180}/_{286}$ of 100 per cent, or 63 per cent, and we thus learn that 63 per cent of crystalline sodium carbonate is water.

Again, the knowledge of molecular weights is imperative in estimating the *proportional weight of substances entering into a chemical reaction.*

For instance, let us calculate the amount of calcium carbonate and hydrochloric acid needed to make calcium chloride.

Such a problem is solved as follows:

We first figure out what the reaction would be, and express same by the appropriate equation.

In this case it is:

$$CaCO_3 + 2\,HCl = CaCl_2 + CO_2 + H_2O$$

$CaCO_3$	+ $2\,HCl$	= $CaCl_2$	+ CO_2	+ H_2O
1 molecule	2 molecules	1 molecule	1 molecule	1 molecule
calcium carbonate.	hydrochloric acid.	calcium chloride.	carbon dioxide.	water.

What are the molecular weights of these several bodies?

$CaCO_3$.

At. wt. of Ca = 40. Ca = 1 × 40 = 40
At. wt. of C = 12. C = 1 × 12 = 12
At. wt. of O_3 = 16. O_3 = 3 × 16 = 48
Mol. wt. $CaCO_3$ = 100

HCl.

At. wt. of H = 1. H = 1 × 1 = 1
At. wt. of Cl = 35.5. Cl = 1 × 35.5 = 35.5
Mol wt. of HCl = 36.5
Hence 2 molecules HCl = 73.0

$CaCl_2$

Ca = 1 × 40 = 40
Cl_2 = 2 × 35.5 = 71
Mol. wt. $CaCl_2$ = 111

CO_2

C = 1 × 12 = 12
O_2 = 2 × 16 = 32
Mol. wt. CO_2 = 44

H_2O

H_2 = 2 × 1 = 2
O = 1 × 16 = 16
Mol. wt. H_2O = 18

To write equation again:

$$\underset{100}{CaCO_3} + \underset{73}{2HCl} = \underset{111}{CaCl_2} + \underset{44}{CO_2} + \underset{18}{H_2O}$$

This summed up means:

100 Gm. absolute calcium carbonate
and 73 " " hydrochloric acid
173 Gm.

Give 111 Gm. calcium chloride.
44 " carbon dioxide.
18 " water.
173 Gm.

Observe that we obtain exactly the same number of grams of new substances as the total amount of material with which we started in. In other words, in chemical reactions matter is not lost, but merely rearranged. (*Law of conservation of matter.*)

It is scarcely necessary to say that the amounts given in the above equation are merely proportional, that in place of 100 Gm. and 73 Gm. given above, we could put 100 pounds and 73 pounds; 100 ounces and 73 ounces; or 100 tons and 73 tons. All that is essential is that quantities of calcium carbonate and hydrochloric acid be in the proportion of 100 to 73.

Let us carry out several modifications of this idea:

(*a*) Suppose the example was: "How much calcium chloride can be made from 1 pound of calcium carbonate?"

From above equation we see that 100 pounds calcium carbonate give 111 pounds calcium chloride. We therefore reason thus:

If 100 pounds $CaCO_3$ give 111 pounds $CaCl_2$, then 1 pound $CaCO_3$ will give $1/100$ of 111 pounds $CaCl_2$, or 1.11 pounds $CaCl_2$.

The same reasoning expressed in proportion reads:

$$100 : 111 :: 1 : x$$

$$x = \frac{111 \times 1}{100} \text{ equals } 1.11.$$

(*b*) Suppose the question was reversed, and read: "How many ounces of calcium carbonate and of absolute hydrochloric acid are needed to make 60 ounces of calcium chloride?"

Since this question asks quantities of the two ingredients, it is in reality two examples, and we must solve each separately.

From the above equation we learn:

100 ounces calcium carbonate and 73 ounces absolute hydrochloric acid make 111 ounces calcium chloride.

Applying this truth to the case under consideration, we reason—

If to make 111 ounces $CaCl_2$ we need 100 ounces $CaCO_3$, then to make 60 ounces $CaCl_2$ we will need $^{60}/_{111}$ times 100 ounces $CaCO_3$,

or $^{6000}/_{111}$ ounces $CaCO_3$,
or 54+ ounces $CaCO_3$.

Or expressed in proportion:

$$111 : 100 :: 60 : x$$

$$x = \frac{100 \times 60}{111} \text{ equals } 54+.$$

The second part of the example is solved by similar reasoning, viz.:

If to make 111 ounces $CaCl_2$ we need 73 ounces absolute HCl, then to make 60 ounces $CaCl_2$ we need $^{60}/_{111}$ times 73 ounces HCl, or $^{4380}/_{111}$ ounces HCl, or 39.46 ounces absolute HCl.

Or expressed in proportion:

$$111 : 73 :: 60 : x$$

$$x = \frac{73 \times 60}{111} \text{ equals } 39.46.$$

(*c*) The figures just given suggest a problem of simple proportion which can be best considered here.

It is seen that the answer just given is 39.46 ounces absolute (100 per cent) hydrochloric acid. Now, 100 per cent hydrochloric acid is a gas, and what we commonly call hydrochloric acid is a solution of this gas in water, the hydrochloric acid directed by the Pharmacopœia being a solution containing between 35 and 37 per cent by weight of the gas (p. 443).

Now, suppose the above example asked: "How much hydrochloric acid U.S.P. is needed to make 60 ounces calcium chloride?"

We have just seen that to make 60 ounces $CaCl_2$ 39.46 ounces 100 per cent HCl is required. Now let us suppose our U.S.P. acid is exactly 36 per cent. If we use this weaker 36 per cent acid it will require a proportionally greater quantity, and indeed $^{100}/_{36} \times 39.46$ ounces or $^{3946}/_{36}$ ounces or 109.6 ounces of 36 per cent hydrochloric acid.

The amount is reasoned out as follows: This part of the problem consists of a combination of alligation and proportion. If we wish to dilute 100 per cent acid to a 36 per cent acid we know (see p. 79) we must dilute 36 ounces of the 100 per cent with enough water to make 100 ounces and even so in our problem each 36 ounces of 100 per cent acid must be replaced by 100 ounces of 36 per cent acid. However, the amount of 100 per cent acid called for in our problem is 39.46 ounces and this will, of course, mean a proportionally larger amount of 36 per cent acid; that is, if for 36 ounces of the 100 per cent acid we must use 100 ounces of 36 per cent acid; then for 39.46 ounces of 100 per cent and we must use $\frac{39.42}{36.00}$ times 100 ounces or 109.6 ounces as shown above. The equation of proportion would be 36 : 100 :: 39.46 : x. x = 109.6.

(*d*) In the same way we can determine the amounts of elements combining to form a compound.

Suppose the question is: "How many grams of zinc and of iodine are needed to make 100 Gm. of zinc iodide?"

The question in this case runs as follows:

$Zn + I_2 = ZnI_2$
Atomic weight of zinc, 65 $Zn = 1 \times 65 = 65$
Atomic weight of iodine, 127 $I_2 = 2 \times 127 = 254$
Molecular weight of $ZnI_2 = 319$

Rewriting the equation:

$$\begin{array}{ccccc} Zn & + & I_2 & = & ZnI_2 \\ 65 & & 254 & & 319 \end{array}$$

This means:

To make 319 Gm. ZnI_2 we need 65 Gm. of zinc and 254 Gm. of iodine. Then to make 100 Gm. ZnI_2 we need $^{100}/_{319}$ times 65 Gm. of zinc and $^{100}/_{319}$ times 254 Gm. iodine, or 20.3 Gm. of zinc and 79.5 Gm. of iodine.

Or by proportion:

As to zinc, $319 : 65 :: 100 : x. \quad x = \frac{65 \times 100}{319} = 20.3.$

As to iodine, $319 : 254 :: 100 : x. \quad x = \frac{254 \times 100}{319} = 79.5.$

Lastly, the knowledge of molecular weights is essential in quantitative analysis, both gravimetric and volumetric. This phase of the question will be left until Chemical Analysis is considered in Chapter LIV.

The writing and balancing of chemical equations, such as those given above, will be explained later (p. 403).

THE NEWER CHEMISTRY

While the foregoing portion of Chapter XXII gives the routine information essential to the pharmacist, the progress made in chemical thought during the last thirty years must be briefly outlined. The difficulty in making such an outline is twofold: first, extended comment on this subject does not properly belong in a text book on pharmacy; and secondly the newer knowledge while important and thought-provoking is at the present time distinctly incomplete and at times even subject to controversy. In the Bibliography found at the end of this chapter a fairly complete list of papers on the subject are offered to those who desire to pursue the subject further.

MOLECULAR STRUCTURE

While molecular weights can be determined in gases and in solutions; while in these forms molecular conditions are supposed to exist; little is known as to the molecular conditions occurring in fluids and in solids. Langmuir, Compton, and others even doubt the existence of molecules in solids, believing that every atom has its position so determined by other atoms that it cannot be said to belong or not to belong to the same molecule as some other atom.

Molecular structure has been the subject of study for eighty years or more. The many graphic or structural formulæ used throughout this book indicate attempts to picture the arrangement of the atoms within the molecule, by means of the so-called "Frankland bonds." The co-valence theories of Lewis, Kossell, and others cited above represent another step in study of molecular formula. Raman (1928) by his study of the spectra lines obtained by passing the light from a mercury arc through liquids and solutions of chemicals pointed the way to experimental determination of molecular structure. Kettering, Shutts, and Andrews from data obtained from the Raman spectra have devised working models of molecules showing vibrations suggestive of the physical activity within the molecule.

ATOMIC STRUCTURE

The discovery of electrons by Thomson in 1897, caused an entire change in our view of atoms. From the former idea that atoms were *particles* of matter that could not be subdivided into anything smaller; that elements were *forms* of matter that could not be broken into anything simpler; we now believe that atoms are the complex systems described below and that the elements as we now know them may be broken into simpler forms. As to the *structure of the atom* we now believe that each atom consists of a *nucleus* about which are placed or around which revolve *electrons.* As to the *nucleus,* Rutherford, Whitney, and others think that its diameter is only $\frac{1}{100,000}$ of the diameter of the atom and that despite this minuteness it constitutes over 99 per cent of the mass of the atom. Harkins believes that while the hydrogen nucleus contains one positive charge of electricity, the nucleus of any other element contains as many charges as the ratio of its atomic weight to the atomic weight of hydrogen. Thus calcium (at. wt., 40) has 40 positive electronic charges in the nucleus. These positive charges are called by Rutherford, *protons.*

As to *electrons,* these are particles of negative electricity that either revolve in circular orbits around the nucleus (Bohr) or are situated on surfaces either spherical or cubical (Langmuir) around the nucleus. These electrons, while larger than the nucleus are infinitely small, Whitney expresses the size by saying that if an atom were a mile in diameter, the electrons would be about the size of a base ball and the nucleus would not be more than a pin head. Harkins believes that the total number of electrons is exactly the same as the number of charges of positive electricity, found in the nucleus; that is the total number of electrons, is the same number as the atomic weight of the elements. Of these electrons however some are in the nucleus and the others revolve around or are in position about the nucleus. Thus an atom of helium is supposed to have in the nucleus 4 protons and 2 electrons, leaving 2 electrons outside of the nucleus; an atom of calcium is supposed to have in the nucleus, 40 protons and 20 electrons, leaving 20 electrons outside of the nucleus. *The position of these outside electrons* has been subject to much interesting discussion. It is rather generally assumed that the first "orbit" or "shell" surrounding the nucleus contains only two electrons; that each succeeding "orbit" or "shell" contains 8 electrons and that the outer orbit contains the residual electrons. Thus in the calcium atom, the 20 electrons mentioned above are distributed, 2 in the innermost "orbit," 8 in the next orbit, while the 10 remaining electrons are distributed either (*a*) 8 in a third "orbit" and 2 in the fourth (outermost) "orbit," or (*b*) all ten in the third (outermost) "orbit." Bohr's application of Planck's quantum theory has replaced the conception of definite orbits by the idea that there are certain regions in the space surrounding the nucleus at which the recurrent of the constantly moving electron is a maximum.

Valence according to the newer ideas, utilizes this principle of the electrons in the outermost "orbit." The ideal number of electrons for the outermost "orbit" is 8. Whitney points out that the neutral elements, neon, argon, and xenon (valence = 0) have 8 electrons on the outer orbit.

On the other hand, the structure of fluorine is something like this: Nucleus, 19 protons, 10 electrons; outside of the nucleus, first "orbit" 2 electrons, outer "orbit" 7 electrons. The outer "orbit" therefore, is, minus 1 electron of the ideal 8; hence fluorine is a negative element of the valence one. Lastly, the structure of sodium may be considered; nucleus, 23 protons, 12 electrons; outside of the nucleus, first "orbit," 2 electrons; outside "orbit" 9 electrons. The outer orbit therefore has 1 more electron than the ideal 8; hence sodium is a positive element of the valence one.

As Whitney quaintly puts it: the combination of a sodium and fluorine means "the liberality of sodium with its one extra electron in accommodating the special avidity of fluorine for just one electron.

This idea has been developed by Lewis, Kossell, Lowry, Sidgewick, Fry, and others into electronic theories of valence and into what Lewis calls co-valency. These theories are still incomplete and unsatisfying; hence, for further particulars, our readers are referred to the Bibliography found at the end of this chapter.

The views of 1920 on atomic structure as described above have been theorized into vagueness and confusion. Armstrong compares the present views on this subject with the Cheshire cat of "Alice in Wonderland" which finally faded into nothing but a "Grin." G. P. Thomson (1929) likens the electron to "a gossamer spider floating through the air at the center of a number of radiating filaments, which control its flight as the air wafts it about."

A recent positive statement available is that of Zehnder (1930) who submits the following postulates as to the nature of matter.

1. The world is built out of substances from which proceed forces.
2. From substance in itself proceed two fundamental forces: gravitation and .... elasticity.
3. The nucleus of the hydrogen atom is spherical.
4. The ether is a substance like all other substances differing from these only quantitatively.
5. The speed of the ether "atom" is about that of the speed of light; the former produces the latter.

6. The ether "atom" is about 17 billion times lighter than the hydrogen atom.

7. The nuclei of the chemical atoms are pressed together by powerful ether pressure.

8. Aggregates of prime atoms receive in ether of sufficient density an ether envelope, thereby becoming chemical atoms.

9. Every chemical atom possesses enormous vibration energy, dwindling to zero at −273° C.

10. Electrical energy is in its essence the "heat of the ether." The electron is a small cloud of ether.

As to the ether, Tombrock revives the old conception plus modifications of the views expressed by Mendelejeff (1902). Tombrock considers the ether as a gas with indivisible atoms, each atom weighing about one-millionth of the hydrogen atom. It is the material out of which ordinary atoms are built.

Recent views as to atom structure as expressed by Crowther, Harkins, Ewing, Compton, Chadwick, Cockcroft, and Walton may be summarized as follows:

1. The *nucleus* consists of protons and electrons, existing in very close combinations now known as *neutrons*. Bartlett expresses his opinion that the protons exist only in the form of neutrons. Perrin believes that the *alpha particles* (the helium nucleus or 4 protons plus 2 electrons) are found in the nuclei of the heavier elements. Other physicists believe that *photons*, which resemble electrons but producing light vibrations, are components of certain nuclei.

2. *Planetary Electrons.*—The outer electron described on page 404 seems more elusive today than it was ten years ago. About all we know is that these outer electrons exist as vibrant entities occupying a large portion of the space within the atom.

3. The mathematical relationships between the protons and the electrons described on page 404 still obtain; Harkins expressing the make-up of the nucleus as $(p_2e)z$; "p" equaling the number of protons; "e" the number of electrons; "z" the atomic number.

Photon.—In explaining the behavior of electrons, physicists have attempted to visualize the *photon* or the "atom of light" as Loring calls it. This conception is used to designate the radiation which issues when an electron falls from one energy level to another. A photon apparently acts in two ways: (*a*) as a particle; (*b*) as a wave. Ewing in his thought-provoking paper on the atom describes the photon as follows:

> "The photon carries a definite quantity of energy and is characterized by a definite frequency of vibration. Its energy depends on the two levels between which the electron falls, and this determines the frequency of the vibration which the photon conveys, for the frequency is equal to the energy divided by that mysterious constant of nature, the quantum of action discovered by Planck. In any element all the atoms have the same set of energy levels: these contribute to the emission spectrum and account for its groups of spectral lines. In heavy atoms there are many energy levels, and consequently very many lines appear in their spectra."

If the photon is at times an essential component of the nucleus, then this idea affords an admirable explanation of plant photosynthesis (p. 650) and of phosphorescent phenomenon (p. 433).

QUANTUM THEORY

This theory should be mentioned since it figures considerably in recent chemical literature as a confirmation of the accuracy of the Bohr atom model. Conceived through entirely mathematical processes by Planck, it has been developed by Bohr and Born and by them applied to the vibrations of atoms and electrons. Reduced to its simplest terms the theory is that atomic energy is emitted, not continuously but in intermittent units or *quanta*, which Planck and Bohr have reduced to a mathematical formula. Those desiring to follow the subject more fully, a list of papers are given in the bibliography at the end of this chapter.

ATOMIC NUMBER

In studying the effect of x-rays upon crystals (see p. 167), Moseley discovered that "the spectra of chemical elements produced by using them as sources of *x*-rays differed one from the other in a very simple progressive numerical manner." From this fact he and other investigators deduced the idea of the *atomic number* which is equal to (*a*) the square root of the frequency of *x*-rays; (*b*) the number of outer electrons in the atom of the element in question; (*c*) the positive charge on the nucleus of the element. What is far more amazing is that experimentation showed that the atomic number of hydrogen is 1, helium is 2, lithium is 3 and so on in regular sequence to uranium with atomic number 92. In this way atomic numbers have furnished a satisfactory explanation of the periodic system.

PERIODIC SYSTEM

Newlands, Mendelejeff and Lothar Meyer indicated that "the properties of elements are periodic functions of their atomic weights." Described in its briefest form, it originally showed that when elements were placed in rows of seven in sequence of their atomic weights viz.:

Li	Be	B	C	N	O	Fl
7	8	11	12	14	16	19
Na	Mg	Al	Si	P	S	Cl
23	24	27	28	31	32	35.5

etc. there resulted a table of seven columns, each column containing elements that closely resembled each other in chemical properties. Thus, the maximum valence of the elements in the seven columns regularly progressed from I in the lithium column to VII in the fluorine-chlorine column; while the usual valence of the elements in the seven columns ran I, II, III, IV, III, II, and I. Moreover, the central (carbon) column included elements that were neither distinctly positive nor negative, while those columns to the left of the carbon column included the positive elements while to the left were the negative elements; the positive or negative character of the elements progressing with the distance the column was from the central column.

This Mendelejeff table, while interesting and attractive was found by no means perfect. Thus an eighth column had to be added for the iron and platinum groups of metals and upon the discovery of the inert gases helium, neon, argon, crypton, and xenon, a new zero column had to be added. There have been published a number of ingenious explanations of why such a table based upon atomic weights was possible but only recently has a plausible explanation been found. It is apparently no mere coincidence that the Moseley atomic number of the element indicates the position of the element on the new periodic table which begins with H (At No. 1) continues like this:

	He	Li	Be	B	C	N	O	Fl	
At. No.	2	3	4	5	6	7	8	9	
	Ne	Na	Mg	Al	Si	P	S	Cl	
At. No.	10	11	12	13	14	15	16	17	etc.

More than this outline cannot be given in this book and for further details the reader is referred to the articles cited in the bibliography at the end of this chapter.

COMPOSITION OF ELEMENTS

On page 384 it was stated that the fixed idea of a score of years ago that our present known elements could not be broken into any simpler forms is now subject to revision. In 1815, Prout advanced the idea that all elements were combinations of either hydrogen or of a hypothetical element of half of the atomic weight of hydrogen called by Prout "protyl." This idea was given favorable consideration for some years but fifty years since was practically rejected by all chemical teachers. The discovery of radium (1898) however reawakened the question of the possible complexity of elements. Soddy has found that the element of the highest atomic weight, uranium (238) spontaneously breaks down successively into radium (224) and then into lead (206); while thorium (232) breaks down to lead (208). By bombarding nitrogen with *x*-rays, Rutherford obtained hydrogen and helium, while Ramsay has reported the disintegration of copper into lithium.

From these data, Rutherford, Harkins, and Soddy deduce that elements are combinations of hydrogen and helium and that Prout's hypothesis is not a fallacy. If Prout was right elements should have round number atomic weights (see p. 386). The fact that supposedly "exact" atomic weights are not round numbers is explained in two ways. Harkins points out that most atomic weights are close to whole numbers when compared to oxygen (O = 16) and he further explains the discrepancy between O = 16 and H = 1.0078 is due to what he calls "the packing effect" which his experiments show is about 0.0078 for most elements. On the other hand, many believe that the reason why "exact" atomic weights are not whole numbers is due to the fact that the elements, as we know them are mixtures of isotopes.

ISOTOPES

These are elemental forms that are chemically identical but have different types of nuclei, thus producing slight differences in atomic weight. Above in discussing the production of lead by the disintegration of other elements, in one line the atomic weight of lead was placed at 206 and in another at 208. This is experimentally true, the first figure applying to lead obtained from uranium, the second to lead from thorium, while ordinary lead as obtained by usual processes of metallurgy and purification has the atomic weight of about 207. Thus it would seem to indicate that ordinary lead was a mixture of the two isotopes of lead 206 and 208 respectively, both types possessing the same atomic number (82). In addition to these isotopes of lead, isotopes of neon (at. wts. 20 and 22) chlorine (at. wts. 35 and 37) and bromine (at. wts. 79 and 81) have been isolated.

IONIC THEORY

Under Solution (p. 140) it was pointed out that when acids, bases and salts dissolve in water the molecules of these substances are separated into electrically charged atoms or atom groups which are called *ions*. The negatively charged ions are called *anions* while the positively charged particles are called *cations*. The chemical subject to ionization is called an *ionogen*, whereas the electrically-conductive solution made from the ionogen is called the *electrolyte*.

Acids are those substances which give hydrogen ions (hydrions) in aqueous solution; bases under the same conditions give hydroxyl ions (hydroxidions); while salts give ions other than hydrions and hydroxidions. Thus an acid like H_2SO_4 dissociates in solution into 2 positive hydrogen ions and one SO_4 ion bearing two negative charges; a base like KOH dissociates into 1 positive potassium ion and one OH ion bearing one negative charge; while a salt like K_2SO_4 dissociates into 2 positive potassium ions and one SO_4 ion bearing two negative charges.

Expressed in equation form

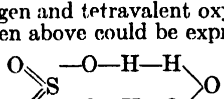
$$H_2SO_4 = \overset{+}{H} + \overset{+}{H} + \overset{--}{SO_4}$$

$$KOH = \overset{+}{K} + \overset{-}{OH}$$

$$K_2SO_4 = \overset{+}{K} + \overset{+}{K} + \overset{--}{SO_4}$$

The degree of ionization not only varies with the composition of the chemical but it also varies in the case of the same chemical according to the dilution of the solution; or according to "the concentration of the solution" as physical chemists put it. Thus in 63 per cent nitric acid only 9 out of 100 molecules are ionized, whereas in 6.3 per cent HNO_3, 83 out of 100 molecules are ionized. In concentrated sulfuric acid (95 per cent) only 7 in 1000 molecules are ionized, whereas in 4.9 per cent H_2SO_4 over half of the molecules are ionized. At the other end of the scale may be cited carbonic acid (17 molecules out of 10,000 ionized); and absolutely pure water, ten million liters of which are supposed to contain only 1.008 Gm. of hydrogen ions and 17.008 Gm. of hydroxyl ions.

During the past decade a number of thoughtful papers on ionization have appeared. The more important of these are cited in the bibliography given at the end of this chapter. Consensus of opinion today (1935) seems to be less favorable to the free ion idea outlined above than to the view that in solutions, ions are in combination with water in hydrated form. Thus Lowry inclines to the belief that the ionization of sulfuric acid really means the dissociation of the acid into $HSO_4.OH_3$ and $SO_4.OH_4$; the groups "OH_3" and "OH_4" being termed *oxonium*. This "oxonium" idea presumes that in hydration, either in ionized solution or in crystals, there is the possibility of H_2O representing divalent hydrogen and tetravalent oxygen according to circumstances. Thus the $HSO_4.OH_3$ formula given above could be expressed graphically as:



CATALYSIS

This is the promotion or the hindering of a chemical action by the presence in the reacting mixture of a chemical (the *catalyst*) which apparently does not enter the reaction. Throughout this book are found numerous cases of catalysis, the application of which has been one of the most notable factors in the progress of industrial chemistry during the last decade. Among the applications may be cited the contact process of making sulfuric acid (see p. 449) the synthesis of ammonia (p. 502) and the hydrogenation of fats (p. 727), and the action of stabilizing catalysts in solution of hydrogen dioxide (p. 417).

The mechanics of catalysis has been the subject of much discussion during the past score of years. Sabatier believes that in all cases of catalysis an unstable intermediate substance is formed (see ether, p. 661). Tweedy describes three theories of catalysis:

(*a*) intermediate compound theory, just outlined; (*b*) adsorption on the surface of the catalyst; (*c*) electronic radiation. Tweedy admits that all three theories have some experimental proof, but does not feel that we can draw final conclusions at this time.

THE PHASE RULE

This is a simple statement that enables us to foretell what operations we can perform upon a system of substances under observation, simply by counting the number of so-called "components" and so-called "phases" present. The number of operations that can be performed is called the Degree of Freedom of the system, and the largest number possible would be three; temperatures could be changed, pressures could be changed, and concentrations (or amounts in a given volume) could be changed. In many cases the phase rule shows us that only two of these can be changed, and in some cases only one or even none at all. The phases which are to be counted are simply the homogeneous layers or strata in the system, such as the liquid water and the vapor in a bottle of water (two phases) or the salt, solution and vapor (three phases) in a vessel of saturated solution. The components, likewise to be counted, are the individual substances from which the system is prepared, as water (one component) in the first example, and salt and water (two components) in the second. The phase rule unites these three ideas in a simple arithmetical equation; the degree of freedom = number of components − the number of phases + 2; or, $F = C - P + 2$.

Hill points out the value of an understanding of the phase rule in pharmacy. Thus the question of the solubility of phenol in water may be easily explained by an application of the rule. It also is of service in solving problems of chemistry such as reversible reactions like

$$CaCO_3 + \text{heat} = CaO + CO_2$$
$$CaO + CO_2 = CaCO_3$$

COLLOIDS

These have been briefly discussed on p. 177 in connection with the pharmaceutical process of dialysis. Further study by physical chemists shows that colloids play an important rôle in many operations of art and nature. This is especially true in the study of solutions (p. 140) which physical chemists now divide into (*a*) *ionic solutions*, (*b*) *molecular solutions*. Some writers prefer calling a colloidal solution a *dispersoid* and the dissolving of colloids *peptization*. This is accomplished by converting substances in the colloidal state, through reduction of the size of their particles. For examples of peptizing methods, see Krantz's "Pharmaceutical Chemistry." In colloidal solutions, the individual particles are larger than molecules and smaller than 0.0001 mm. in diameter. These particles usually bear electric charges which are usually negative. By reducing solids down to extremely minute conditions of subdivision colloidal solutions of normally insoluble matter may be obtained; thus dialyzed iron (p. 571) is a colloidal solution of ferric hydroxide; while colloidal solutions of silver, of gold, of selenium, and of sulfur are known. The two official colloidal silver preparations, *argentum proteinicum forte* and *argentum proteinicum mite* are considered as dispersoids of silver oxide rather than of elemental silver. Such colloidal metallic solutions are apt to precipitate upon standing unless substances like gelatin, proteids or gums are present. Such substances so used are called *protective colloids*. It is now assumed that in colloidal combinations, *adsorption* (p. 156) plays an important part. Bancroft explains the action of anesthetics, narcotics, and certain poisons in terms of the reversible coagulation of the colloids of the brain and of the sensory nerves.

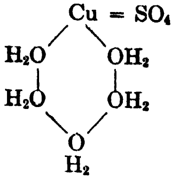
Colloidal substances in contact with water and with other solvents have the property of forming *gels*. According to Hatschek, there are four types of gels; (*a*) reversible, such as gelatin which can be changed from the jelly to the liquid form by use of suitable heat; (*b*) nonreversible, such as hydrated silica gel (p. 549) which does not return to the liquid form after gelatinization; (*c*) special types of organic chemicals which are soon changed from gels into crystalline precipitates; (*d*) a little studied group represented by collodion films or membranes. It is now thought that in these gels there is a definite combination of the colloid with the molecules of the solvent.

Physical chemists explain many chemical phenomena as manifestations of the colloidal condition. On the other hand, eminent chemists with less inclination toward physics, such as Armstrong, vigorously oppose such ideas.

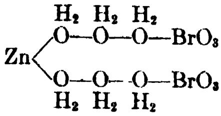
CRYSTALLOIDS

These have been mentioned on p. 177 in the chapter on crystallization. For many years physical chemists have sought a solution to the riddle of water of hydration; why certain chemicals, such as potassium iodide crystallize without crystal water; why sodium sulfate crystallizes with 10 molecules of water; and why sodium phosphate crystallizes with 12 molecules of water. Is the water a loosely molecular attachment or can it be expressed by valence in the graphic formula of the chemical?

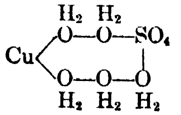
Rakuzin attempts to answer this question by assuming the possibility of tetravalent oxygen (p. 417) and tetravalence copper in crystals of copper sulfate and suggests that the graphic formula of $CuSO_4.5H_2O$ may be:



Similarly Barker suggests for zinc bromate, $ZnBrO_3.6H_2O$, the graphic formula:



which readily leads to the assumption that $CuSO_4.5H_2O$ may be



BIBLIOGRAPHY

Molecules.—(Size) Anon., Merck's Rep., 14, 1905, 350; Hollemann-Cooper, 1912, 50; Mack, Sci. Monthly, 33, 1931, 365.

Molecules and Crystal Structure.—Noyes, Jl. Frank. Inst., 185, 1918, 59; Compton, Jl. Frank. Inst., 185, 1918, 745; Whitney, Jl. Ind. Eng. Ch., 12, 1920, 599.

Atomic Theory.—Meyer-McGowan, 1906, 196; Dewar, Ch. and Dr., 82, 1913, 20; Thomson, Ch. and Dr., 84, 1914, 903; Cockshott, Ph. Jl., 58, 1897, 61.

Atomic Structure.—Thomson, Phil. Mag., 46, 1898, 528; Ph. Jl., 90, 1913, 211, 251, 294, 329, 368 and 406; Jl. Frank. Inst., 195, 1923, 737 and 196, 1923, 1 and 145; "Beyond the Electron," 1928; Phil. Mag., [7], 6, 1928, 1254. Millikan, Science, 32, 1910, 436 and 59, 1924, 473; Rutherford, Phil. Mag., 10, 1905, 163; 21, 1911, 669; 27, 1914, 488; Science, 58, 1923, 209; Proc. Roy. Soc., A123, 1929, 373; *ibid.*, A136, 1932, 735; Eve, Jl. Frank. Inst., 179, 1915, 269; Crehore, Phil. Mag., 29, 1915, 310; Phil. Mag., through C.A., 16, 1922, 377, 2448 and 2634; Soddy, Chem. News, 117, 1918, 147, 158 and 169; Lodge, Ph. Jl., 102, 1919, 230; Langmuir, Jl. Am. Ch. Soc., 41, 1919, 868; Nature, through C.A., 14, 1920, 3572; Am. Dr., 68, Oct., 1920, 25; Science, 54, 1921, 59; C.A., 16, 1922, 2253; Whitney, Jl. Ind. Eng. Ch., 12, 1920, 599; Darwin, Nature, through Radium, 16, 1921, 53; Browne, Ph. Jl., 107, 1921, 4; Harkins, Jl. Am. Ch. Soc., 37, 1915, 1367 and 1383; Science, 50, 1919, 577; Jl. Frank. Inst., 194, 1922, 165, 329, 521, 645 and 783 and 195, 1923, 67; Jl. Am. Ch. Soc., 54, 1932, 1254; McLennan, Science, 55, 1922, 219; Aston, Jl. Frank. Inst., 193, 1922, 581; Allen, Jl. Soc. Ch. Ind., 42, 1923, 338; Jeans, *ibid.*, 42, 1923, 1105; Bragg, *ibid.*, 42, 1923, 690; Crowther, Ph. Jl., 112, 1924, 270 and Scientia, 39, 1926, 163; Smith, Jl. Soc. Ch. Ind., 44, 1925, 115 and 229; Dingle, Jl. Soc. Ch. Ind., 44, 1925, 602 and 621; Editorial, *ibid.*, 45, 1926, 873; Patrick, Ph. Jl., 120, 1928, 105; Fischer-Treuenfeld, C.A., 22, 1928, 4284; Eddington, Nature, 124, 1929, 840; Proc. Roy. Soc., A134, 1931, 524 and "The Nature of the Physical World," 1929; Tombrock, Ch. News, 140, 1930, 23, 66, 98, 165 and 212; G. D. Thomson, Jl. Soc. Ch. Ind., 48, 1929, 311; Zehnder, Zt. Phys., 63, 1930, 706; Flint, Jl. Soc. Ch. Ind., 49, 1930, 309; Armstrong, *ibid.*, 49, 1930, 491; Pauling, Jl. Am. Ch. Soc., 53, 1931, 1367; Dushman, Jl. Ch. Ed., 8, 1931, 1074; Loring, Jl. Soc. Ch. Ind., 51, 1932, 288; Ewing, Science, 76, 1932, 199; Perrin, Compt. rend., 194, 1932, 1343; Fournier, *ibid.*, 194, 1932, 1482; Daniels, Science, 81, 1935, 523.

Atomic Weight.—Gray, Jl. Soc. Ch. Ind., 45, 1926, 435 and 51, 1932, 556; Partington, *ibid.*, 45, 1926, 453; Finter, *ibid.*, 45, 1926, 454.

Molecular Structure.—Bartlett, Science, 76, Aug., 26, 1932, Supp., p. 8.

Avogadro's Law.—Avogadro, Jl. de phys. (1811), through L. Meyer, 1888, 8; Cannizaro, Miolati, Ch. Zt., 34, 1910, 593; Anon., Ch. and Dr., 76, 1910, 734.

Valence.—Herz., Ch. Zt., 30, 1906, 1273 and 1284; Werner, Zt. Elektrochem., 17, 1911, 601; Stark, Zt. Elektrochem., 17, 1911, 514; Frankland, Ch. News, 2, 1860, 27; Ann. Chim. Pharm., 85, 1852, 329; Freud, Ch. News, 97, 1908, 171; Falk and Nelson, Jl. Am. Ch. Soc., 22, 1910, 1637; 8th Inter. Cong. App. Ch., 6, 1912, 212; *ibid.*, Jl. Am. Ch. Soc., 37, 1915, 274; Whitney, Jl. Ind. Eng. Ch., 12, 1920, 599; Langmuir, Science, 44, 1921, 59; Allen, Jl. Soc. Ch. Ind., 42, 1923, 338; Noyes, Proc. Am. Phil. Soc., 66, 1927, 287.

Co-valence.—Cranston, Jl. Soc. Ch. Ind., 44, 1925, 37; Prideaux, *ibid.*, 44, 1925, 25; Sidgewick, *ibid.*, 46, 1927, 799; Cranston, *ibid.*, 47, 1928, 208; Drew, *ibid.*, 47, 1928, 949; Fry "Electronic Conception of Valence" and C.A., 23, 1929, 1564; Pauling, Jl. Am. Ch. Soc., 53, 1931, 3225.

Berzelius' Affinity Theory.—Schweigger's Jl., 6, 1812, 119.

Atomic Number.—Van Den Broeck, Phil. Mag., 25, 1913, 740; Moseley, C.A., 8, 1914, 463 and 2307; Harkins, J. Am. Ch. Soc., 37, 1915, 1367; Science, 50, 1919, 577; Jl. Frank. Inst., 194, 1922, 165, 329, 521, 645, 783 and 195, 1923, 67; Soddy, Ch. News, 117, 1918, 158 and 169; Darwin, Nature, through Radium, 16, 1921, 53; Browne, Ph. Jl., 107, 1921, 4.

Periodic System.—Mendelejeff, Mon. sci., 1879, through Ch. News, 40, 1879, 231, 243, 255, 267, 279, 291, 303, *ibid.*, 41, 1880, 2, 27, 39, 49, 61, 71, 83, 93, 106, 113, 125; Crookes, Ch. News, 54, 1886, 115; Eccles, Dr. Circ., 31, 1887, 28; Arny, Am. Dr., 61, 1913, 75; Darwin, Nature, through Radium, 16, 1921, 53; Browne, Ph. Jl., 107, 1921, 4.

Composition of Elements.—Prout (1815), see Veleys Ch. News, 49, 1884, 185 and Gerber, *ibid.*, 51, 1885, 64; Ramsay, Jl. Ch. Soc., 101, 1912, 1367 and 103, 1913, 264; Arny, Am. Dr., 61, 1913, 75; Soddy, Ch. News, 117, 1918, 147, 158 and 169; Rutherford, Radium, 18, 1923, 309.

Isotopes.—Soddy, Ch. News, 117, 1918, 147, 158 and 169; *ibid.*, 118, 1919, 85, 97 and 109; Darwin, Nature through Radium, 16, 1921, 53; Aston, Jl. Frank. Inst., 193, 1922, 581; Harkins, Jl. Frank. Inst., 1922 and 1923 (see above); Jl. Am. Chem. Soc., 54, 1932, 1254; Millikan, Science, 69, 1929, 481; Loring, Ch. News, 144, 1932, 70.

Ionic Theory.—Arrhenius, Zt. ph. Ch., 1, 1887, 631; also Jl. Am. Ch. Soc., 34, 1912, 353; Walden, C.A., 5, 1911, 413; Thomson, Nature, through Ph. Jl., 93, 1914, 697; Stroup, A.J.P., 92, 1920, 81; Brockman, Jl. Soc. Ch. Ind., 44, 1925, 501; Editorial, *ibid.*, 46, 1927, 870; Kendall, Science, 66, 1927, 610; Lowry, Jl. Soc. Ch. Ind., 47, 1928, 1233; Cady and Elsey, Jl. Ch. Ed., 5, 1928, 1425; Foerster, Zt. angew. Ch., 41, 1928, 1013; Walker, Jl. Soc. Ch. Ind., 47, 1928, 536; Schwarzenbach, C.A., 25, 1931, 1428; Flint, Jl. Washington Acad. Sci., 22, 1932, 97.

Oxonium Compounds.—Armstrong, Jl. Soc. Ch. Ind,. 46, 1927, 494; Smith and Goehler, Jl. Ind. Eng. Ch., anal. ed., 3, 1931, 58.

Electrolytes and Ionogens.—Blum, C.A., 19, 1925, 1221; Foerster, Zt. angew. Ch., 41, 1928, 1013.

Catalysis.—Berzelius, 61, 1836, 150; Armstrong, J. Soc. Ch. Ind., 41, 1922, 258T, Bancroft, Jl. Ind. Eng. Ch., 14, 1922, 326, 444, 545 and 642; Sadtler, A.J.P., 95, 1923; 270; Tweedy, Jl. Soc. Ch. Ind., 45, 1926, 157 and 177; Firth, *ibid.*, 45, 1926, 251; Taylor, *ibid.*, 45, 1926, 447; Sabatier, Jl. Ind. Eng. Ch., 18, 1926, 1005; Jl. Soc. Ch. Ind., 46, 1927, 681 and 702; Downs, *ibid.*, 45, 1926, 188T; Editorial, *ibid.*, 37, 1928, 21; Lippmann, Ch. Zt., 53, 1929, 22; Leffman, Jl. Frank. Inst., 207, 1929, 282; Armstrong, Jl. Soc. Ch. Ind., 49, 1930, 177; Frolich, Jl. Ind. Eng. Ch., 23, 1931, 1366.

Phase Rule.—Gibbs (1874–78) through Findlay, The Phase Rule, 1923, 5; Hill, Am. Dr., 69, June, 1921, 28.

Quantum Theory.—Planck, Nature, 106, 1920, 508; Bohr, C.A., 7, 1913, 3712; Jeans, Ch. and Dr., 91, 1919, 457; Valentiner, C.A., 15, 1921, 3927; Adams, Bull. Nat. Research Council, Vol. 7, Part III, 1923, No. 39; Haas, "Quantum Chemistry," 1930; Dushman, Jl. Ch. Ed., 8, 1931, 1074; Loring, Jl. Soc. Ch. Ind., 51, 1932, 287.

Acids.—Graham, Phil. Trans., 2, 1833, 255 and Tilloch's Jl., 80, 1833, 451.

Bases.—Couch, A.J.P., 95, 1923, 533.

Acids, Bases and Salts.—Cady and Elsey, Jl. Ch. Ed., 5, 1928, 1425; Bjerrum, C.A., 26, 1932, 3716.

Colloids.—Ostwald, Grundriss der Kolloid Chemie., 1907; Stevenson, Am. Dr., 56, 1910, 309; Freiman, Zt. angew. Ch., 24, 1911, 2420; Ostwald, Zt. Ch. Ind. Kolloid through C.A., 5, 1911, 1704; Bechhold, Zt. angew. Ch., 25, 1912, 1197; Zsigmondy, 8th Int. Cong. App. Ch., 22, 1912, 263; Wimmer, Jl. A.Ph.A., 3, 1914, 1004; Bradbury, Jl. Frank. Inst., 176, 1913, 319; Bancroft, J. Phys. Ch. through C.A., 9, 1915, 3739; Jl. Frank. Inst., 185, (1918) 29, 199 to 73; Jl. Ch. Ed., 8, 1931, 2374; Alexander, Jl. Soc. Ch. Ind., 39, 1920, 270R and Jl. Ind. Eng. Ch., 14, 1922, 800; Whitney, Jl. Ind. Eng. Ch., 12, 1920, 599; Loewen, Ch. Zt., 46, 1922, 449; Scoville, Bull. Pharm., 37, 1923, 188; Kermack, Jl. Soc. Ch. Ind., 44, 1925, 401; Bragg, *ibid.*, 44, 1925, 70; Slater, *ibid.*, 44, 1925, 499T; McBain, *ibid.*, 45, 1926, 490; Von Veimarn and co-workers, C.A., 22, 1928, 4028; DeWaele, *ibid.*, 24, 1930, 3152; Editorial, Jl. Soc. Ch. Ind., 48, 1929, 419; Hatschek, *ibid.*, 48, 1929, 389; Sargent, Ch. and Dr., 112, 1930, 613; Lorenz, Paper Ind., 12, 1930, 267; Bary, C.A., 25, 1931, 858; Haller, *ibid.*, 26, 1932, 18; Lupton, Ch. and Dr., 116, 1932, 199.

Crystals and Water of Hydration.—Barker, Jl. Soc. Ch. Ind., 44, 1925, 19T; Rakuzin, C.A., 23, 1929, 1323; Gibbs, Pre-print. Inst. Ch. Eng., 1930.

CHAPTER XXIII

THE NEGATIVE ELEMENTS AND THEIR COMPOUNDS

On page 389 we learned that the elements were roughly divided into the two classes, the negative elements and the positive elements, according to their behavior when submitted to electrolytic action. We have also seen that the hydroxides of the negative elements are called acids, the hydroxides of the positive elements are called bases, while the union of the acids and bases results in a class of compounds called salts.

The salts, along with the bases, will be considered under the metal they contain, and the acids will be considered in the next chapter, as it is advisable, before proceeding to a consideration of the official acids, to study the negative elements from which the important acids are derived, as well as those recognized by the Pharmacopœia.

The negative elements are also called the nonmetallic elements, or metalloids. The nonmetals rarely possess a metallic appearance, are usually poor conductors of electricity, and combine with hydrogen to form gaseous bodies.

A list of the negative elements of importance in pharmacy is found on p. 390, while the following table shows those recognized by the Pharmacopœia either as the free element or in combination other than in acids or in salts. In this list the negative metals, arsenic and antimony, are not mentioned, since their analytic behavior groups them among the metals, and they can there be more profitably discussed.

Oxygen (O):
- Water, H_2O.
- Distilled water, H_2O.
- Sterilized distilled water, H_2O.
- Solution of hydrogen dioxide (containing about 3 per cent of H_2O_2).

Chlorine (Cl):
- Chlorinated lime, U.S.P. X (containing not less than 30 per cent available chlorine).
- Solution of sodium hypochlorite (containing between 4 and 6 per cent of NaOCl).
- Surgical solution of chlorinated soda (containing between 0.45 and 0.5 per cent available chlorine).

Iodine (I):
- Tincture of iodine (containing about 7 per cent iodine).
- Mild tincture of iodine (containing about 2 per cent of iodine).
- Compound solution of iodine (containing about 5 per cent iodine).
- Ointment of iodine (containing 7 per cent iodine).

Sublimed sulfur (S):
- Washed sulfur.
- Precipitated sulfur.

Nitrogen monoxide (N_2O).

Phosphorus (P):
- Pills of phosphorus, U.S.P. X (6/10 of 1 mg. to a pill).

Carbon:
Wood charcoal, U.S.P. X.
Purified animal charcoal, N.F. VI.
Activated charcoal, U.S.P. XI.

Carbon dioxide.

Boric acid (H_3BO_3).

Purified siliceous earth (a form of SiO_2)

Hydrogen and *Helium* are not recognized by the U.S.P. but both are worthy of notice at this place.

HYDROGEN

Hydrogen is produced in the laboratory by treatment of certain acids with certain metals (see p. 534). In commerce many cheaper methods of production are used (see Bibliography at end of this chapter).

It is a colorless, odorless, and tasteless gas, and is interesting as being the lightest known substance. By reason of this fact it is chosen by chemists as the standard of atomic weight and of a large number of other chemical and physical measurements.

Beside ordinary hydrogen (H_2) monatomic and triatomic hydrogen are now known. Urey, Murphy, and Brickwedde (1931) obtained from ordinary hydrogen small quantities of the isotope (see p. 406) having the atomic weight of 2. This heavy hydrogen has been called "deuterium" by Lawrence.

HELIUM

Helium should be mentioned because of its interesting history. Noted first in 1868, by Lockyer in the sun's atmosphere, it was discovered in 1895, by Ramsay in the mineral clevite. It remained a laboratory curiosity until 1918 when it was found in the natural gas of Texas, Oklahoma and Kansas, from which it was extracted for use as a noninflammable gas for war balloons.

From this source almost 10,000,000 cubic feet of the gas was extracted during the year ending July 1, 1930. It has been obtained by Taylor by heating monazite sand.

OXYGENIUM—Oxygen

(Oxygen)

Symbol, O. Atomic weight, 16

Oxygen contains not less than 99 per cent by volume of O. For convenience it is usually supplied in compressed form in metallic cylinder.

Summarized Description:

Colorless, odorless, tasteless gas; soluble in 34 volumes of water and 3.6 volumes of alcohol. For details see U.S.P., p. 274. For *tests for identity*, for *impurities* (carbon dioxide, halogens, acids, alkalis, oxidizing substances) and for *assay*, see U.S.P., p. 274.

Remarks.—Oxygen, while used a number of years in medicine is now official; having been given pharmacopœial recognition in U.S.P. IX. It can be made by treating potassium chlorate alone or preferably a mixture of that chemical with manganese dioxide; the latter catalyst being added to prevent too rapid evolution of the gas. A modern method of extemporaneous preparation of oxygen is by inserting a perforated can of sodium peroxide (*oxone*) into water contained in a suitable metallic generator.

Oxygen may also be produced by passing chlorine over slaked lime in the presence of a catalyst (nickel hydroxide). The lime is converted into bleaching powder and each molecule of $Ca(OCl)_2$ found therein produces 2 atoms of oxygen (Sweeny).

It is also made commercially from *Plumboxan* ($Na_2MnO_4:Na_2PbO_3$) by heating same at 500° to 550° C. Most of the commercial oxygen is now prepared by the distillation of liquid air or by the electrolysis of water.

Oxygen is a colorless, odorless, and tasteless gas, which is noninflammable, but one of the best supporters of combustion. Its use in medicine is becoming more extended day by day, it being used to aid respiration in extreme cases where the lungs refuse to absorb ordinary air. For such emergency cases a good quality of oxygen is absolutely necessary, and it behooves the pharmacist to arrange to procure the gas with little loss of time. The manufacture of the gas for such purposes by the pharmacist is rarely practicable, and, moreover, scarcely necessary, inasmuch as the various firms in different portions of the country will furnish an excellent quality of oxygen in compressed (liquid) form at a comparatively low figure.

Ozone, O_3, is an allotropic form of oxygen. It is usually prepared by passing air through an "ozonizing tube," in which the oxygen of the air by action of the so-called "silent discharge" of electricity is condensed to ozone. Ozonizing tubes are now sold for the purpose of purifying the air in houses. Whether the ozone really purifies the air is a matter of dispute.

AQUA (N.F. VI)—Water

Potable water (H_2O) conforming to the description and tests summarized below:

Summarized Description.

A clear, colorless, practically tasteless, and odorless liquid. Solids, not more than 3 parts to 10,000. For details see N.F. VI, p. 50. For *tests for identity*, for *impurities* (organic matter, lead, copper, iron, chlorides, nitrites, nitrates, ammonium compounds) see N.F. VI, pp. 50 and 51.

Remarks.—The U.S.P. XI originally omitted aqua from its texts because all preparations were directed to be made with distilled water. However, after the book was issued it was found that directions to use distilled water in percolating extracts, fluidextracts, etc., and in making certain other preparations were unnecessary. An interim revision statement was therefore issued permitting use of water (for which N.F. standards will suffice until the U.S.P. standards are issued in the next periodic supplement). For further discussion see "Remarks" under Aqua Redestillata N.F. VI.

AQUA DESTILLATA—Distilled Water

(Aq. Dest.)

Water (H_2O) purified by distillation.

Preparation.—No method given in U.S.P. X and XI. U.S.P. IX method was to distil 1000 volumes of water, throw away the first 100 volumes of distillate, collect the next 750 volumes and throw away the residue left in the still.

Summarized Description.—Colorless, clear, liquid without odor or taste. A *p*H of not less than 5.8 and not more than 7 with methyl red and bromthymol blue respectively is required in the tests for purity. For details see U.S.P., pp. 65 and 66. For *tests for identity*, for *impurities* (sulfates, chlorides, calcium, metals, ammonia, carbon dioxide, solids) see U.S.P., pp. 65 and 66.

AQUA DESTILLATA STERILISATA—Sterilized Distilled Water (Aq. Dest. Steril.)

Condensed Recipe.

Place freshly distilled water, neutral to litmus, in a flask of hard glass, stopper the flask with a plug of cotton wrapped in gauze; close top of flask with a piece of nonabsorbent paper or tinfoil and sterilize in a steam autoclave (p. 183) at 115° C. for thirty minutes. In the absence of an autoclave the water may be sterilized by boiling for one hour. For details see U.S.P., p. 66.

Storage.—Sterilized distilled water, when stored in a stoppered container, should be used within twenty-four hours after its distillation. If stored in an hermetically-sealed container it should conform to the *tests for sterility of liquids* (U.S.P., p. 469).

AQUA REDESTILLATA (N.F. VI)—Redistilled Water

(Aq. Redest.—Double-distilled Water, Triple-distilled Water)

Redistilled Water is water (H_2O) purified by repeated distillation.

Redistilled water is free from nonvolatile matter and gases; also from microorganisms or other oxidizable matter.

Condensed Recipe.

Distil distilled water, U.S.P., previously treated with potassium permanganate, T. S. and sodium hydroxide, T. S. from a special distillation flask of resistant glass provided with all-glass condenser with ground glass joint. Test each 50 cc. of the distillate with Nessler's reagent (p. 501) until the test is negative. Then collect the ammonia-free distillate in 500 cc. sterile flasks. For details see N.F., p. 53.

Summarized Description.—No description given in N.F. except hydrogen-ion concentration tests (p. 1034) and tests for residue (0.0005 Gm. per 100 cc.) and for the following impurities, sulfate, chloride, calcium, metals, ammonia, carbon dioxide, and oxidizable substances. For details see N.F., p. 53.

Remarks.—There are now four official forms of water—*Aqua*, N.F. VI, *Aqua Destillata*, U.S.P. XI, *Aqua Destillata Sterilization*, U.S.P. XI, and *Aqua Redestillata*, N.F. VI. Throughout this book it is customary to discuss the official substances of the Pharmacopœia in the large type in which these words are printed and the official substances of the Formulary in smaller type. However, as the four official forms of water are so closely interconnected, it seems wise to consider all of them together.

Considerable surprise has been expressed over the deletion of *Aqua* from U.S.P. XI. This action was brought about largely by the papers by LaWall, who argued that at its best ordinary potable water is scarcely pure enough to meet the requirements of modern pharmacy and that *Aqua Destillata* has become so readily accessible and is of such reasonable price, that there is no excuse for using ordinary water any longer. This argument is not universally conceded; hence the action of the National Formulary in retaining *Aqua* for the ordinary uses of pharmacy. As just mentioned, *Aqua* is supposed to represent potable water furnished by the ordinary source of supply, and is, therefore, not so pure as distilled water. The question of the water supply of cities is one receiving much attention at the present time, but it is beyond the limits of this volume to enter into a complete discussion of the subject. It is assumed that the water supplied by a municipality shall be potable; *i. e.*, not merely containing a minimum of the inorganic salts, but also free from the bacteria which enter it through sewage contamination. Former Pharmacopœias provided a test for the limit of organic matter in the potassium permanganate test, it directing that 100 cc. when mixed with 10 cc. of diluted sulfuric acid and brought to the boiling point should not discharge the color imparted to the solution by the addition of 0.4 cc. of decinormal potassium permanganate solution, even after boiling for ten minutes. In N.F. VI, the purity of water is determined by those other tests; in conjunction with three other tests recognized by the Pharmacopœia—the phenolsulfonic acid test for nitrates, the sulfanilic acid test for nitrites, and the Nessler test for ammonia. In water analysis the last is the most important chemical test for sewage contamination. In the thorough application of this test the water is distilled from an alkaline solution and then from alkaline permanganate solution, whereby any nitrogenous matter present in the water is converted into ammonia, which is detected by treating the distillate with Nessler's reagent. (See p. 501.) This reagent will produce either a yellow coloration or a brown precipitate, according to the amount of ammonia present, and from the extent of coloration has been evolved a scheme for the quantitative estimation of the albuminoid ammonia present in the water. These chemical tests are of value merely in establishing the fact of sewage contamination, and it may here be said that the simple fact of such contamination would be of little danger were the sewage free from the numerous bacteria which cause disease. Of the bacteria causing mischief in potable water, the most dangerous are the typhoid and colon bacilli. In closing the subject mention may be made of the fact that the best method of water purification is by filtration through deep layers of sand. (See p. 155.) The U.S.P. X and N.F. VI intend that *aqua* should be potable water in its purest obtainable state, and such water, after having been proved potable, is permitted to be used by the pharmacist in much of his manufacturing. A water may be hygienically pure and yet contain salts, the presence of which, while nowise affecting the potability of the water, would seriously interfere with the use of such water in the manufacture of chemicals. For this reason the careful pharmacist must use in all prescription work distilled water, the price of which is now so low that its general use is not an extravagance.

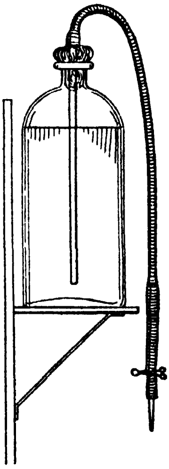


Fig. 256.—Distilled-water holder

Distilled water is made by taking a thousand volumes of water, distilling it from a suitable apparatus, rejecting the first 100 volumes which come over, then collecting the subsequent 750 volumes. It will be seen by this process that the first 100 and the last 150 volumes of water are thrown away, the intermediate portion being the only part considered fit for use. The explanation of this procedure is found in the fact that ordinary water is usually impregnated with gaseous substances, such as carbon dioxide and possibly ammonia, and that these gases will pass over with the first 100 volumes; hence this portion is thrown away. The same water contains also solid matter, various salts, and possibly fixed organic material, and this remains in the still, and the provision of former Pharmacopœias against complete evaporation of the water from the residue is to prevent charring, with the subsequent evolution of empyreumatic matter.

Redistilled water just introduced into the National Formulary is a double or triple distilled water required in the manufacture of sterile solutions in ampuls. It will be discussed under *Ampullæ* (p. 990).

The tests for distilled water are much more severe than for ordinary water. For instance, while the formerly official permanganate test applied to ordinary water is that the tint should not be discharged after boiling 100 cc. of water with 0.4 cc. of decinormal permanganate solution for ten minutes, distilled water was directed to be mixed with 0.1 cc. decinormal potassium permanganate solution (one quarter the quantity).

In the storing of distilled water more care should be taken than is usually observed. Tightly corking bottles of distilled water generally results in the development, in the water, of microscopic plants, consisting of many varieties of cryptograms, including *Penicillium glaucum* and a number of algæ. Experience has shown that if the water is kept in bottles which are loosely stoppered with a pledget of cotton, such growths are not so frequent. At the prescription counter a capital way of handling the water is to place it in a ½-gallon, wide-mouthed bottle on the shelf, 6 or 7 feet above the floor. A syphon consisting of a bent glass tube with flexible rubber tube at the end, the rubber tube terminating with a tapering glass tube and provided with a pinchcock, is placed in the water, the orifice of the bottle being closed with cotton. When water is desired, all that is necessary is to open the pinchcock and allow the water to syphon into the bottle or graduate, which can then be held on a level with the eye without the necessity of raising the heavy water receptacle (Fig. 256).

Sterilized distilled water is a new official form of water designed to furnish that fluid chemically and bacterially pure. The pharmacopœial monograph, read in connection with the chapter on sterilization as found in the Pharmacopœia and in this book (Chap. LII) will furnish the information needed by the student.

Heavy Water.—On a preceding page we referred to *heavy hydrogen*. Lewis has separated from ordinary distilled water, very small quantities of heavy water consisting of 2 atoms of heavy hydrogen and 1 atom of heavy oxygen (atomic weight 17 or 18). This heavy water in now available in small amounts for experimental purposes.

LIQUOR HYDROGENII PEROXIDI—Solution of Hydrogen Peroxide

(**Liq. Hydrog. Perox.**—Liquor Hydrogenii Dioxidi U.S.P. X, Solution of Hydrogen Dioxide)

Solution of Hydrogen Peroxide is an aqueous solution containing, in each 100 cc., not less than 2.5 Gm. and not more than 3.5 Gm. of H_2O_2.

Storage.—Preserve in a cool place protected from light and dust. If the stopper of the bottle is coated with paraffin or replaced by a pledget of purified cotton, deterioration is retarded.

Summarized Description.

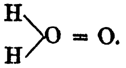
Colorless, liquid, usually odorless, acid taste, froths when held in mouth, prone to deterioration. Must not contain more than 0.05 Gm. per 100 cc. of preservative. For details see U.S.P., p. 213. For *tests for identity*, for *impurities* (nonvolatile matter, excess of acid, arsenic, heavy metals, hydrofluoric acid, barium and oxalic acid) and for *assay* see U.S.P., pp. 212 and 213.

Remarks.—Hydrogen dioxide was discovered by Thenard in the year 1818, and is recognized by the Pharmacopœia in the form of a 3 per cent solution under the name of Liquor Hydrogenii Peroxidi, formerly "Dioxidi." Hydrogen dioxide is now known in highly concentrated form (90 to 100 per cent). The latter is a liquid that explodes when heated to 151° C.

Perhydrol is the trade name given a 30 per cent solution of hydrogen dioxide. Modern electrochemical methods now produce a 60 per cent dioxide on a commercial scale. This solution is now transported in Europe in carboys in carload lots.

Hyperol is the trade name for a solid compound of the dioxide and urea, containing 35 per cent of H_2O_2.

The formula H_2O_2 has given rise to considerable discussion as to the structure of this body. At the first glance it seems to lead to the conclusion that either oxygen has the valence I or hydrogen has the valence II. An explanation, intended to cover the usual valences of these two elements is that the body consists of two hydroxyl groups, viz., HO—OH. This, however, is combated by several investigators, who claim that if such a linkage were true, the oxygen would be more tightly combined in this body than it is in water, while the reverse is true. Others claim that the graphic formula of hydrogen dioxide is



$$\begin{matrix} H \\ & \rangle O = O. \\ H \end{matrix}$$

that is, it exhibits one atom of tetravalent oxygen; while still others think it represents water with an extra atom of oxygen very loosely attached thereto. According to Geib and Harteck, commercial peroxide contains both forms of H_2O_2.

The official solution of hydrogen dioxide is prepared by treating barium dioxide with phosphoric acid. The usual method of manufacturing, however, is by substituting for the phosphoric acid the cheaper sulfuric acid. The equation of manufacture from sulfuric acid is as follows:

$$BaO_2 + H_2SO_4 = H_2O_2 + BaSO_4$$

From this will be seen that the barium dioxide is converted into the insoluble barium sulfate, from which the solution of hydrogen dioxide can be removed by simple filtration.

Patents have been issued for the production of hydrogen dioxide by other methods, such as obtaining it as a by-product in the electrolytic manufacture of persulfuric acid. None of these methods have as yet been commercially successful.

The official solution should contain not less than 2.5 per cent H_2O_2 and, upon proper treatment, 1 volume of the solution should yield 10 volumes of oxygen; for this reason the official solution is frequently called "10 volume peroxide."

The Pharmacopœia provides an assay of hydrogen dioxide, based on the quantity of potassium permanganate solution required to oxidize the same.

The official solution is a clear, colorless liquid, having a slightly acidulous taste, producing a peculiar sensation and a soapy froth in the mouth. It is odorless or has an odor resembling ozone. This peculiar sensation is due to its oxidizing action on the mucous membrane and its excretions. Its chemical and medical action is based entirely on the amount of oxygen that it gives up under such conditions, and it may be here said that the solution, giving off its oxygen on standing, deteriorates rapidly. Not only this, but the evolution of oxygen in tightly-closed bottles is sometimes so considerable as to cause an explosion. Hence it is advisable to avoid an overtight stopping of the bottle, unless the latter is very stout. Manufacturers preserve hydrogen dioxide solution by the addition of a small amount of acetanilid and the present pharmacopœial test for limit of preservative gives tacit approval of the custom. Such chemicals as acetanilid and other substances that preserve the solution, even when present in minute quantities, are now considered as *stabilizing catalysts* (p. 407).

Hydrogen dioxide is used in medicine as an antiseptic, and in the arts as an oxidizer. An illustration of the latter application is the custom, formerly in vogue, of bleaching dark hair a golden tint by the application of hydrogen dioxide. The disastrous effects of the continued treatment of this kind are now so well known that it is used less than it formerly was for this purpose.

Dose.—4 cc. (1 fluidrachm).

THE HALOGENS

By the halogens we mean the four elements, chlorine, bromine, iodine, and fluorine. The word halogen is derived from two Greek words, *als*, which means a salt, and *eidos*, which means a likeness, the phrase being coined to illustrate the similarity of the compounds of these elements to salt, sodium chloride, which is taken as the type of haloid salts.

CHLORINE

Symbol, Cl. Atomic weight, approximately 35.5

This element derives its name from the Greek word *chloros*, which means green, because of the greenish-yellow tint of the gas itself. Chlorine was isolated by Scheele in 1774, who obtained it from hydrochloric acid by treatment similar to that now in vogue in its manufacture. By reason of its origin Scheele called the new substance *dephlogisticated muriatic acid*, because he concluded it represented hydrochloric acid which had been freed from phlogiston, that hypothetic element which played so important a part in the chemical philosophy of the eighteenth century. Scheele considered the substance a compound, and it was not until 1810 that Sir Humphrey Davy proved it was an element, and by him it was named chlorine. In 1920, Harkins separated chlorine into two isotopes (see p. 406).

Chlorine is manufactured for pharmaceutic purposes by treatment of hydrochloric acid with manganese dioxide, in which case the reaction is as follows:

$$4HCl + MnO_2 = 2H_2O + MnCl_2 + Cl_2.$$

In practice, for the hydrochloric acid a mixture of common salt and sulfuric acid is usually substituted, the chemical action being by either of the following equations, according to relative proportion of chemicals used:

$$(a)\ 2NaCl + 2H_2SO_4 + MnO_2 = Na_2SO_4 + MnSO_4 + 2H_2O + Cl_2.$$
$$(b)\ 2NaCl + 3H_2SO_4 + MnO_2 = 2NaHSO_4 + MnSO_4 + 2H_2O + Cl_2.$$

This process has the advantage over the first process in avoiding loss of hydrochloric acid, for it will be noticed that when hydrochloric acid is used, half of it goes to make manganese chloride, while in the second process the metals combine with the less expensive sulfuric acid.

An economic modification of the first process is found in *Weldon's regenerative process*, which consists in treating the manganese chloride with lime in the presence of air, the reaction being as follows:

$$MnCl_2 + 2CaO + O = CaCl_2 + CaMnO_3.$$

From the calcium chloride thus produced hydrochloric acid can be obtained, and from this the chlorine can be easily isolated, while from the calcium manganate, manganese dioxide is produced.

Chlorine is used so largely in the arts that the isolation of the element is one of the great industries, especially in England. As in the case of such industries, persistent efforts are made to obtain more satisfactory and cheaper processes of manufacture. The Weldon regenerative process, above cited, was an illustration of the ingenuity used in attempting to cheapen the production of this staple; and investigators turned their efforts to the obtaining of chlorine without the use of the comparatively expensive manganese salt. One chemical process of this character, which has the advantage of being practically continuous, is the *Deacon process.* In this process bricks or other porous pieces of earthenware are impregnated with a saturated solution of the sulfates of copper and sodium; after heating to redness in a furnace the vapors of hydrochloric acid are passed over them. The following reaction ensues:

$$(a)\ CuSO_4 + 2HCl = CuCl_2 + H_2SO_4.$$

The sulfuric acid of the above reaction is condensed, and is thus saved. The bricks, impregnated with copper chloride, are then heated in a current of air, the reaction being as follows:

$$(b)\ CuCl_2 + O = CuO + Cl_2.$$

The chlorine vapors are then passed into the desired condensing agent, be it water or lime, while copper oxide remains in the brick. The bricks are then heated in a current of hydrochloric acid, the reaction being:

$$(c)\ CuO + 2HCl = CuCl_2 + H_2O,$$

and the water is allowed to escape as steam. It will be seen that the bricks are impregnated once more with copper chloride, and from that time on they are treated with successive applications of air and hydrochloric acid vapor by the reactions *b* and *c*. Thus a comparatively small quantity of copper salt may be used to convert tons of hydrochloric acid into chlorine.

Of late chlorine has been produced by electrolytic methods; passing electricity through a solution of sodium chloride, contained in cells in which porous diaphragms separate the anodes (positive poles) from the cathodes (negative poles). The salt solution (brine) flows into the anode compartment breaking into chlorine (which emerges as gas from the anode compartment) and into hydrogen and sodium hydroxide (alkali), which pass through the diaphragms into the cathode compartments (Fig. 257).

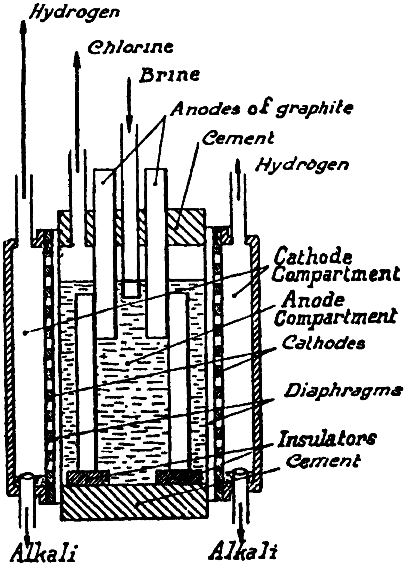


Fig. 257.—Electrolytic cell for isolating chlorine.

A method of obtaining chlorine at the prescription counter is by the treatment of potassium chlorate with hydrochloric acid. The reaction might be expressed by the following equation:

$$KClO_3 + 6HCl = KCl + 3H_2O + 3Cl_2.$$

It is, however, more complex than is suggested by the above equation for various oxides of chlorine are produced at the same time. This reaction is used for the extemporaneous manufacture of a preparation similar to chlorine water, and it constitutes the recipe for *compound solution of chlorine,* N.F. V. For some years it was a popular prescription in several sections of the country, the physician prescribing, instead of chlorine water, a solution of potassium chlorate containing hydrochloric acid. According to the method in which this prescription is compounded two very different results are obtained. If the potassium chlorate is dissolved in water and the hydrochloric acid added to the diluted solution, we obtain merely an acid solution of potassium chlorate. On the other hand, if the powdered potassium chlorate is placed in a bottle, the prescribed quantity of hydrochloric acid added, and the bottle allowed to stand corked a minute or two, the yellow fumes of chlorine are evolved, and on filling the bottle with water a variety of chlorine water is obtained. In receiving such a prescription the careful pharmacist is frequently in a quandary as to which method he shall pursue. In the writer's experience, several physicians objected to the chlorine water. Therefore the only way out of the dilemma is to call the attention of the prescriber to the two possibilities, and ask which result is desired. It is usual, however, that the method in which the chlorine is easily evolved is the desired method of compounding the prescription.

The Medical Use of Chlorine.—This represents but a small tithe of its commercial value, it being safe to say that tons of chlorine are used for bleaching and manufacturing purposes, where pounds of chlorine are used in the healing art. In medicine the use of chlorine is chiefly as a disinfectant.

Disinfectants are those bodies which destroy offensive organic matter—material which by decomposition breeds disease. Most disinfectants are oxidizing agents, but chlorine is particularly interesting because it in itself is not a complete oxidizing agent. To be an oxidizing agent a body should contain oxygen which it can give up. Oxygen, of course, is not found in chlorine, but this energetic element performs the function by borrowing oxygen of its neighbor in this manner:

$$5Cl_2 + 5H_2O = HClO_3 + 9HCl + O_2.$$

In other words, chlorine acts as an oxidizing agent only in the presence of water.

The above statement also explains the bleaching action of chlorine. The use of chlorine as a bleach was discovered by Berthollet in the year 1788, and the process proved so much more satisfactory for the finishing of textile fabrics than sun-bleaching, then in vogue, that its use soon became extended. At first the various cloth factories produced their own chlorine used in bleaching, but since the manufacture of chlorine was a matter so different from that of the manufacture of cloth, it soon fell into the hands of experts. The transportation of the chlorine to the cloth manufacturers soon became a serious matter. In those days the compression of gases had not reached the stage of perfection that now obtains, and at first the only practical method of dispensing was in the form of an aqueous solution, and the transportation of the large quantity of the water necessary to hold the small quantity of chlorine rendered this plan practically prohibitive. The problem of a practical method of transportation of chlorine was found by Tennant, in the year 1799, in his discovery of chlorinated lime, it being found that freshly burnt lime was capable of absorbing as much as 35 to 40 per cent of its weight of chlorine. From that time on the cloth manufacturers made use of this bleaching powder, and the manufacture of this chemical is now one of the most important industries in England. Chlorine is now marketed in liquid form either in steel cylinders or in tank cars. In pharmacy it is used either as chlorinated lime, as solution of chlorinated soda or as chlorine water.

Liquor Chlori Compositus (N.F. V) is prepared by warming together in a flask hydrochloric acid and potassium chlorate and after the evolution of chlorine is accomplished cold distilled water is added to the mixture. The finished product, which contains about 0.4 of 1 per cent of chlorine (0.35 Gm. to 100 cc.) should be freshly prepared whenever wanted.

Aqua Chlori (U.S.P. 1890) was a saturated aqueous solution of chlorine gas (0.4 per cent); the gas being produced by the action of manganese dioxide on hydrochloric acid.

Calx Chlorinata (U.S.P. X) or *chlorinated lime*, or *bleaching powder* is a product resulting from the action of chlorine upon calcium hydroxide, and yields not less than 30 per cent of available chlorine.

It is a white, or gray-white granular powder, smelling of chlorine which deliquesces and decomposes on exposure and is partly soluble in water and alcohol, entirely soluble in diluted acetic acid with liberation of chlorine.

The requirement of the Pharmacopœia of 1890 (35 per cent of available chlorines was unduly high, experience showing that practically no chlorinated lime of strength greater than 30 per cent can be found in the drug market; hence at later revisions the requirement was cut to 30 per cent. As mentioned above, chlorinated lime is made by the passage of chlorine gas over slaked lime, the process being carried on, on a large scale, by passing the gas into specially constructed chambers in which the lime is arranged in different layers on special racks.

Chlorinated lime should not be called "chloride of lime," for it is not chloride of lime; that (or, more correctly, calcium chloride) having the formula $CaCl_2$. Some authorities give the formula of chlorinated lime as $CaOCl_2$, which gives the idea of a definite chemical compound, which the body is not. It is a loose indefinite mixture of calcium chloride, $CaCl_2$, and calcium hypochlorite.

What is calcium hypochlorite? The calcium salt of hypochlorous acid, which comes from hypochlorous oxide.

And what is hypochlorous oxide? That oxide of chlorine in which the element shows its lowest valence.

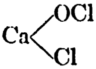
And what is the valence of chlorine?

The valence of chlorine is I, III, V, and VII.

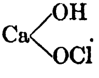
In hypochlorous oxide chlorine has the valence I, hence the formula of the oxide (oxygen having valence II) is Cl—O—Cl or Cl_2O. Hypochlorous acid is made by adding water to the oxide—$Cl_2O + H_2O = H_2Cl_2O_2 = 2HClO$. Calcium has the valence II—1 atom replaces 2 hydrogen atoms of an acid. Since hypochlorous acid, HClO, has but 1 hydrogen atom and 2 are needed, we double the formula, making it, as above, $H_2Cl_2O_2$, and replacing the 2 hydrogen atoms by 1 calcium atom we get $CaCl_2O_2$, or, as it is usually written, $Ca(OCl_2)$. This is the formula of calcium hypochlorite.

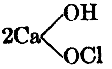
Chlorinated lime is a mixture of calcium chloride ($CaCl_2$) and calcium hypochlorite (CaO_2Cl_2). Let us add these—

Calcium chloride . .	$Ca\ Cl_2$
Calcium hypochlorite .	$Ca\ O_2Cl_2$
The sum is	$Ca_2O_2Cl_4$, or $2CaOCl_2$, for which the graphic

formula  $Ca{<}^{OCl}_{Cl}$ has been assigned.

There are few chemicals regarding whose composition there has been more discussion and less resultant knowledge. Besides the two formulas just given, there have been a number of other suggestions as to its composition.

Thus, in order to explain why a large residue of calcium hydroxide is left when the chemical is extracted with water (for a mixture of calcium chloride and calcium hypochlorite would be completely soluble), it has been claimed that chlorinated lime is a mixture of calcium chloride with a body  $Ca{<}^{OH}_{OCl}$. This body is supposed to dissociate when treated with water as follows:



$$2Ca{<}^{OH}_{OCl} = Ca(OCl)_2 + Ca(OH)_2.$$

Ochi's work convinces him that a carefully prepared chlorinated lime contains as its principle constituent $Ca(OCl)Cl, H_2O$; Neumann and coworkers incline to the formula, $3Ca(OCl)Cl.CaO.6H_2O$; while O'Connor favors $2Ca(OCl)_2.2CaCl_2.3Ca(OH)_2.4H_2O$. Neumann explains these discrepancies by: (*a*) purity of the starting materials; (*b*) percentage of water presence; (*c*) age of sample examined.

H.T.H. is a true calcium hypochlorite. It is a stable free-flowing powder containing 65 per cent of available chlorine. It is marketed in 4-pound tins and in drums of 110 pounds.

Calcium hypochlorite, $Ca(OCl_2)$, contains 49.6 per cent of chlorine, yet H.T.H. is advertised as yielding 65 per cent of "*available*" *chlorine*. Likewise a calculation of the actual chlorine content of bleaching powder would indicate somewhere around 15 per cent of chlorine and yet U.S.P. X directed that it yielded 30 per cent of available chlorine. This anomaly is explained by the fact that when these chlorinated products are used as oxidizing agents (as in liberating iodine from potassium iodide) 1 atom of chlorine liberates 2 atoms of iodine as shown in the following equation:

$$\overset{\substack{\text{Hypochlorous}\\ \text{acid}}}{HOCl} + 2KI + HCl = 2KCl + I_2 + H_2O.$$

$$\left\{\begin{matrix}\text{containing}\\ \text{1 atom of}\\ \text{chlorine}\end{matrix}\right\} \text{—————————} \left\{\begin{matrix}\text{liberates}\\ \text{2 atoms}\\ \text{of iodine}\end{matrix}\right\}$$

Chlorinated lime is used as a general disinfectant. Enormous quantities are now employed for the purification of the public water supply. Customers should be warned to open tin boxes of chlorinated lime cautiously. There have been recently several cases of injury due to the sudden expansion of the gas on opening the can, followed by a shower of lime dust, striking the eyes and face of the victim.

LIQUOR SODII HYPOCHLORITIS—Solution of Sodium Hypochlorite (Liq. Sod. Hypochlor.)

Solution of Sodium Hypochlorite contains not less than 4 per cent and not more than 6 per cent of NaOCl.

Caution.—This solution is not suitable for application to wounds.

Storage.—Preserve in well-stoppered bottles, in a cool place and protected from light.

Summarized Description.

Pale greenish-yellow liquid having a slight odor of chlorine. For details see U.S.P., p. 220. For *tests for identity* and for *assay*, see U.S.P., p. 220.

Remarks.—The old pharmaceutical, *Liquor Sodæ Chlorinatæ*, or Labarraque's solution, described on the next page, has been replaced by this stronger solution of chlorinated soda. Labarraque's solution should contain not less than 2.6 per cent of NaOCl; the new official solution is to contain from 4 to 6 per cent of NaOCl. For the preparation of Labarraque's solution see the next page. Elvove (1910) suggested the preparation of Labarraque's solution by passing chlorine gas through solution of sodium hydroxide of the proper strength. This method is now utilized on a factory scale for preparing hypochlorite solutions containing 14 to 15 per cent of "available" chlorine. The new official solution of 4 to 6 per cent strength is made either by the Elvove process or by use of "H.T.H." It represents a more stable solution than the old Labarraque solution and is of sufficient purity to permit its use in preparing Dakin's solution.

The pink color that Labarraque's solution sometimes exhibits is due to slight traces of manganese arising from the manganese dioxide used in producing the chlorine. When the chlorine used is produced electrolytically this trouble does not occur.

The old type of solution of chlorinated soda is called *Labarraque's solution*, after the French pharmacist, who devised the original formula. *Javel water*, or solution of chlorinated potassa, was the original preparation, but experience showed Labarraque's solution to be the more satisfactory preparation; hence Javel water has fallen into disuse in many parts of this country. Note that these two preparations are called solutions of *chlorinated* soda and potassa, with the express intention of emphasizing the uncertainty of the chemical character, and it may be here stated that these two preparations, as well as the chlorinated lime above mentioned, are now considered as irregular solutions of chlorine in the alkalis rather than as definite chemicals.

LABORATORY EXERCISES

MAKE SOLUTION OF CHLORINATED SODA

Recipe—Monohydrated sodium carbonate	7.0 Gm.
Chlorinated lime	10.0 Gm.
Water, a sufficient quantity,	
To make	100 Gm.

Triturate the chlorinated lime (which should contain not less than 30 per cent of available chlorine) with 20 cc. of water, gradually added, until a uniform mixture results. Allow the heavier particles to subside, and transfer the thinner, supernatant portion to a filter. Then triturate the residue again with 20 cc. of water, transfer the whole to the filter, and, when the liquid has drained off, wash the filter and contents with 10 cc. of water. Dissolve the monohydrated sodium carbonate in 30 cc. of hot water, and add this solution to the previously obtained filtrate contained in a suitable vessel. Stir or shake the mixture thoroughly, and, if it should become gelatinous, warm the vessel very gently until the precipitate subsides. Then transfer the mixture to a new filter, and, when no more liquid drains from it, wash the filter and contents with enough water to make the product weigh 100 Gm. Keep the solution in well-stoppered bottles, protected from light, and in a cool place.

Explanation.—The chemical reaction involved in the above process runs in two equations, since the chlorinated lime employed is a mixture of calcium hypochlorite and calcium chloride:

Equation A:

Calcium hypochlorite	plus	Sodium carbonate	give	Calcium carbonate	plus	Sodium hypochlorite
$Ca(OCl)_2$	+	Na_2CO_3	=	$CaCO_3$	+	$NaOCl$

Equation B:

Calcium chloride	plus	Sodium carbonate	give	Calcium carbonate	plus	Sodium chloride
$CaCl_2$	+	Na_2CO_3	=	$CaCO_3$	+	$NaCl$.

The result of the reaction is a liquid containing sodium hypochlorite and sodium chloride in solution and calcium carbonate (precipitated chalk) as a sediment.

The *equations given above are purposely left incomplete.* Complete these, so that the amount of each element on the two sides of the sign of equality is the same.

Calculations.—Chlorinated lime, being of variable quality, the molecular quantities cannot be conveniently worked out.

However, figure out:

How many grams of chlorine in 10 Gm. of 30 per cent chlorinated lime?

How many grams of chlorine in 100 Gm. of 2.4 per cent solution of chlorinated soda?

Comparison of these figures will show that the pharmacopœial process anticipates the conversion of the chlorinated lime into solution of chlorinated soda with the loss of but 10 per cent of the volatile chlorine—a thing that is theoretically possible, but rarely practically attained.

Remarks on Process.—The recipe of U.S.P. X differs from the one given above in the fact that chlorinated lime is made into a paste with water and to this unfiltered paste the sodium carbonate solution is added, after which the mixture is filtered. This improvement was suggested by the writer and his coworkers. (See Bibliography on p. 438.)

Put chlorinated lime in mortar and triturate with the water.

The *thinner supernatant portion* (see p. 164) contains the soluble part of the chlorinated lime, and this is passed through the filter first. This is an illustration of decantation.

The *heavier particles* are triturated with more water, adding the water gradually with firm pressure of the pestle in order to reduce particles to a pasty condition.

Pour the entire paste on the filter, and thus dissolve the soluble portion left in the chlorinated lime after the first washing.

Use the last 10 cc. water to wash out mortar and to extract the insoluble part of the chlorinated lime contained on the filter.

Dissolve the sodium carbonate in the water in pint flask, and to this add the chlorinated lime filtrate.

If gelatinous, warm, but that only slightly, lest a large amount of chlorine be driven off.

Filter mixture into a tared 8-ounce wide-mouthed bottle. Both solution of chlorinated soda and also chlorinated lime contain chlorine in a form so loosely combined that the gas easily escapes. Hence in the entire process care should be taken to avoid undue exposure, either to the air or to heat.

LIQUOR SODII HYPOCHLORITIS DILUTUS—Diluted Solution of Sodium Hypochlorite

(Liq. Sod. Hypochlor. Dil.—Liquor Sodæ Chlorinatæ Chirurgicalis U.S.P. X, Modified Dakin's Solution)

An aqueous solution of chlorine compounds of sodium containing, in each 100 cc., not less than 0.45 Gm. and not more than 0.50 Gm. of NaOCl, equivalent to not less than 0.43 Gm. and not more than 0.48 Gm. of available Cl.

Storage.—Preserve in well-stoppered bottles, in a cool place and protected from light.

Condensed Recipe.

Made by diluting 1000 cc. of solution of sodium hypochlorite with 5000 cc. of distilled water and then adding thereto 40 cc. of a 5 per cent solution of sodium bicarbonate. The solution must then be tested for neutrality with phenolphthalein and finally assayed and diluted to proper NaOCl content. Full details, see U.S.P., p. 220.

Summarized Description.

Colorless or faintly yellow liquid; slight odor of chlorine. For details see U.S.P., p. 221. For *tests for identity,* for *impurities* (maximum and minimum alkalinity) and for *assay,* see U.S.P., p. 221.

Remarks.—This product was found by Dr. Carrel during his surgical work in the French Army during the World War to be the most satisfactory wound dressing. It cannot be made by diluting Labarraque's solution, since the latter is crudely prepared whereas Dakin's solution must be made with the utmost nicety. Its strength must be carefully adjusted between 0.43 and 0.48 per cent available chlorine. If less than 0.43 per cent, it lacks antiseptic value; if over 0.48 per cent it is irritating to an open wound. Its alkalinity must also be properly adjusted; the Pharmacopœia giving tests for both maximum and minimum alkalinity.

Dakin's solution is quite unstable and must not be dispensed when more than seven days old. Cullen and Hubbard recommend as a stabilizing catalyst (p. 407) 0.5 per cent of borax.

BROMINE

Symbol, Br. Atomic weight, approximately, 80

Bromine (U.S.P. VIII; N.F. V) was isolated by Balard in 1826 from water of the Mediterranean. On account of the very irritating odor it possesses, the discoverer named it after the Greek word *bromos,* which means a stench. Bromine is made from the bromides by a process analogous to that for the isolation of chlorine—*i. e.,* by treatment of the bromide with sulfuric acid and manganese dioxide—a sufficient quantity of acid is added so that at the end of the reaction the manganese will be of the form of a sulfate, thus insuring complete isolation of the bromine. As the source of bromine a native brine called *bittern* is generally used. This bittern is found in various sections of the world, one of the chief sources of supply being salt wells, found in the Saginaw Valley of Michigan. This bittern contains sulfates, bromides, and chlorides of the alkalis, chiefly of magnesium, and a crude concentration of the brine causes the crystallization of the less soluble sulfates and chlorides, leaving a mother liquid consisting chiefly of magnesium bromide. From this mother liquid bromine is obtained by the following reaction:

$$MgBr_2 + MnO_2 + 2H_2SO_4 = MgSO_4 + MnSO_4 + 2H_2O + Br_2.$$

In addition to the explanation of the reaction given above it need only be added that the bromine, on distilling from the reacting mixture, is condensed in earthenware worms, and enters the market after purification by redistillation.

Considerable bromine is produced as a side-product in the German potash industry and, at present, most American bromine is produced by the Dow process, which consists essentially of the electrolysis of magnesium bromide. In Europe it is usually produced by trickling the bittern down through a suitable tower apparatus, up through which rises chlorine gas and steam. The bromine is collected at the top of the tower by use of a suitable condenser.

A 25 per cent solution of bromine in potassium bromide solution is known as *Smith's solution of bromine* and was official in N.F. IV as *liquor bromi.*

Bromine is a very heavy brown liquid, specific gravity 3.000, boiling at about 59° C., having a disagreeable and irritating odor. The corrosive action of its vapor renders it necessary to use care in handling, as it is apt to cause injury to the mucous membrane of the nose and throat and also to the delicate tissue of the eye. Because of this, it has to be shipped in small glass containers, each packed in a tin canister packed with an inert adsorbent such as chalk or infusorial earth. The liquid, bromine, is decidedly caustic, hence the operator must be careful to avoid dropping same on his hands or face.

It is, of course, largely used in the preparation of the very popular bromides. On treating a solution of soda with bromine we obtain solution of sodium hypobromite, which is analogous to the Labarraque's solution just described, and is used instead of Labarraque's solution in determination of urea.

IODUM—Iodine

(Iod.)

Symbol, I Atomic weight, 126.92

Iodine contains not less than 99.5 per cent of I.

Storage.—Preserve in glass bottles closed with stoppers resistant to corrosion and in a cool place, protected from light.

Summarized Description.

Bluish-black rhombic plates, having metallic luster; distinctive odor; acid taste; sp. gr. 4.66; stains skin brown; soluble in 2950 parts of water, in 10 parts of alcohol, in aqueous solution of potassium iodide. For details see U.S.P., p. 196. For *tests for identity,* for *impurities* (cyanogen, chlorine, bromine) and for *assay* see U.S.P., p. 197.

Remarks.—This element was discovered by Courtois in the year 1811, and the discovery was announced by Clement before the National Institute November 29, 1813. It was named by Gay-Lussac (1813) after the Greek word *ioeidos,* meaning violet, on account of the violet tint of its vapor. Iodine was formerly obtained entirely from the ashes of marine plants. In some sections of the world, notably the North of Ireland and on the Scotch coast, these weeds were collected in considerable quantities, and after being dried, were burned, the ashes being called "*kelp*" in Ireland, and "*varec*" in Normandy. These ashes contain iodides, and by treatment with manganese dioxide and sulfuric acid they yield iodine by either of the following reactions:

(a) $2KI + MnO_2 + 2H_2SO_4 = K_2SO_4 + MnSO_4 + 2H_2O + I_2$.
(b) $2KI + MnO_2 + 3H_2SO_4 = 2KHSO_4 + MnSO_4 + 2H_2O + I_2$.

In both these cases the iodine is separated by sublimation.

In other sections, other methods of isolation are employed, such as treatment of the ashes with chlorine, nitrous acid, ferrous and copper sulfates. Moreover, processes are now in vogue in which an infusion of the seaweed is used instead of the ashes, these later and more economic processes being devised in order that the European product might compete with the great modern source of iodine, the niter beds of Chile.

The niter consists chiefly of sodium nitrate (the so-called "Chile saltpetre"). This is obtained from the ore by lixiviation, and the saline solution is concentrated to the point at which the sodium nitrate will crystallize.

The mother liquor from this crystallization contains sodium iodate, which is obtained by evaporating the liquid to dryness. Iodine is isolated from this impure iodate, $NaIO_3$, by treatment with sodium sulfite and bisulfite, the reaction being:

$$2NaIO_3 + 5NaHSO_3 = 3NaHSO_4 + 2Na_2SO_4 + H_2O + I_2.$$
$$2NaIO_3 + 3Na_2SO_3 + 2NaHSO_3 = 5Na_2SO_4 + H_2O + I_2.$$

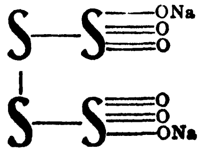
In all these South American processes except the last the crude iodine is separated from the other products by filtration. It is then purified by sublimation.

Iodine is a blue-black, metallic-appearing solid, insoluble in water, but soluble in a solution of potassium iodide, in alcohol, in ether and chloroform, the solution in the two last solvents having a pink to purple color according to concentration. It is quite volatile, hence it must be preserved in well-closed bottles, and by reason of its volatility it is usually purified by sublimation, hence the trade name of the best quality of iodine is *resublimed iodine.*

The test for iodine is the fact that it turns mucilage of starch an intense blue-black color. This is now considered as an adsorption (see p. 156) rather than a chemical reaction although Murray claims that a molecular compound, $(C_6H_{10}O_5)_xI_5$, is obtained. When this test is applied for the detection of iodides it is necessary to liberate the iodine by treatment with some substance containing free chlorine. The iodides form a characteristic yellow precipitate of silver iodide when treated with a solution of silver nitrate, and this precipitate, unlike similar precipitates from chlorides and bromides, does not dissolve in ammonia water. The aqueous and alcoholic solutions of free iodine have a brown tint, and such solutions are decolorized by treatment with sodium thiosulfate (hyposulfite, see p. 493), the equation being:

$$I_2 + 2Na_2S_2O_3 = 2NaI + Na_2S_4O_6.$$

Both products of the reaction just given—sodium iodide and sodium tetrathionate—are colorless, and the latter chemical has the graphic formula—



The word "tetrathionate" means literally "four-sulf-ate," *tetra* being Greek for "four," and *thion* means "sulfur" in the same language.

This decolorization of iodine by sodium thiosulfate is frequently utilized in preparing the so-called *decolorized tincture* of iodine; an unsavory mixture of iodides and organic sulfur compounds. A recipe of this character was given in N.F. IV, but in the preparation of N.F. V., a radical modification of recipe was made, the present method of manufacture being the bleaching out of a solution of iodine in potassium iodide by the action of stronger ammonia water and the final addition, after bleaching, of enough alcohol to make a tincture containing approximately 50 per cent C_2H_5OH. The reaction between iodine and ammonia is quite complicated; the possible resulting products being ammonium iodide, ammonium hypoiodite, ammonium iodate, nitrogen iodide, ammonium formate and even ethylamines. The two last mentioned are the results of interaction between the alcohol and the stronger ammonia water in the presence of the iodine products.

In making the radical change in recipe—using stronger ammonia water as bleaching agent instead of sodium thiosulfate—the Revision Committee of the National Formulary also wisely changed the name of the preparation from the misleading title, *decolorized tincture of iodine*, to the more accurate *tinctura iodidorum*, or *tincture of iodides* (p. 256).

The property of sodium thiosulfate of decolorizing iodine is applied for the quantitative estimation of that element and its derivatives. For this purpose a volumetric solution of sodium thiosulfate is dropped into the iodine solution until the latter is decolorized. In order sharply to distinguish the end reaction, a starch paste is used as an indicator, the blue-black tint in the mixture being discharged the moment a sufficient quantity of the volumetric solution is added (see Chapter LV.)

Iodine and iodides have been found of great value in goiter (see p. 488). The element in the form of a 2 per cent tincture is now largely used as an antiseptic (p. 248).

Dose.—10 mg. (1/6 grain).

TINCTURA IODI—Tincture of Iodine

(Tr. Iodi)

An alcoholic solution of iodine and potassium iodide containing, in each 100 cc., not less than 6.5 Gm. and not more than 7.5 Gm. of I, and not less than 4.5 Gm. and not more than 5.5 Gm. of KI

Storage.—Preserve in glass bottles, closed with stoppers resistant to corrosion, and in a cool place, protected from light.

Condensed Recipe.

Dissolve 70 Gm. iodine in a concentrated aqueous solution of 50 Gm. potassium iodide. Then add enough alcohol to make 1 liter. For details see U.S.P., p. 400.

Assay.—See U.S.P., p 401

Remarks.—Tincture of iodine is an alcoholic solution containing 7 per cent of iodine, 5 per cent of potassium iodide and 5 per cent of added water. The addition of the iodide was suggested by LaWall, as a means of preventing loss of iodine strength of the tincture, as iodine in simple alcoholic solution is partly converted into hydriodic acid and such a tincture on assay will show a deficiency of free iodine. The LaWall plan is a success, as a tincture so prepared, on standing, becomes actually stronger in iodine, due to evaporation of the alcohol. This tincture should be kept in glass-stoppered bottles. Both cork and rubber are attacked by the tincture.

Tincture of iodine is now so largely used as an external antiseptic that the warning must be sounded that it is dangerous to use it in connection with mercuric chloride dressings, for in such event, highly irritating mercuric iodide is produced.

The other official preparations of iodine are: *mild tincture of iodine* (p. 248), *compound solution of iodine,* which contains 5 per cent of iodine dissolved in water by aid of 10 per cent of potassium iodide (p. 210); and the *ointment of iodine*, which contains 4 per cent of iodine and 4 per cent potassium iodide, rubbed with glycerin and a base consisting of wool fat, yellow wax, and petrolatum (p. 368). The National Formulary recognizes *ampuls of iodine* (p. 990).

SULFUR

Symbol, S. Atomic weight, approximately 32

This element has been known from ancient times, the name being of Latin origin, derived from two words, *sal* (salt) and *pyr* (fire). Sulfur is found in the free state in the neighborhood of volcanoes, it being emitted through these from the interior of the earth. It is also found very widely distributed in combination, for example, *gypsum*, which is calcium sulfate, *iron pyrites* (ferrous sulfide), and *galena* (lead and silver sulfide). The commercial source of sulfur is chiefly crude brimstone, which is obtained either from the sides of volcanoes or else mined in certain sections of the world, as for example, extensive deposits of sulfur in Louisiana and Texas.

Sulfur is extracted from the Louisiana mines by sinking a 10-inch pipe down through the sulfur deposit, sending down through the large pipe a 6-inch pipe passing through a cap fitted to the large pipe and then pumping superheated water down through the large pipe. The heat of the water melts the sulfur, while the pressure forces the fused sulfur through the other tubes into vats or ponds, where it solidifies.

The crude volcanic sulfur is roughly purified by straining and pouring into iron molds. Such sulfur comes into the market in cylindric pieces, 1 or 2 feet long and 2 or 3 inches in diameter, under the name of *roll sulfur* or *brimstone.* A purer commercial form is *sublimed sulfur* or *flowers of sulfur*, which is made by putting brimstone in cast-iron retorts and collecting the vapors in large, well-cooled chambers, on the floors of which sulfur falls in the form of fine powder. Sulfur is also obtained as a by-product in the Leblanc process (p. 483).

Sulfur is a lemon-yellow body, and according to whether it is rolled sulfur or sublimed sulfur, is in lump or powder form. This is one of the several forms which the element assumes. Thus, if brimstone is fused and let stand until a pellicle forms on the surface of the fused mass, and then the liquid portion is poured off, the element is found in the form of *yellow prismatic crystals.*

A third form which the element assumes is prepared by taking either the crystals or the rolled sulfur, and heating it in a crucible to a temperature of 160° C., when it is poured into cold water, forming an elastic, rubber-like mass called *amorphous sulfur.* Flowers of sulfur also contains a yellow amorphous sulfur that is insoluble in carbon disulfide. These four widely different bodies are sulfur and nothing else, and it is now supposed to differ in having differing number of atoms of sulfur in the different molecules. Several elements are known to possess this same characteristic of assuming different forms, and such a phenomenon is called *allotropism.*

The official forms of sulfur are:

SULFUR SUBLIMATUM—Sublimed Sulfur

(**Sulfur Sublim.**—Flowers of Sulfur)

Sublimed Sulfur, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of S.

For complete monograph, see p. 31.

SULFUR LOTUM—Washed Sulfur

(Sulfur Lot.)

Washed Sulfur, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of S.

Storage.—Preserve in well-closed containers.

Condensed Recipe.

Mix 100 Gm. sifted sublimed sulfur with 100 cc. of water, add 10 cc. of ammonia water and macerate three days. Then dilute with more water, throw mixture on strainer and wash with water until washings do not turn red litmus blue. Then dry and sift. For details see U.S.P., p. 366.

Summarized Description.

Fine yellow powder, responding to the tests for sublimed sulfur. For details see U.S.P., p. 366. For *tests for identity*, for *impurities* (limit of acid or alkali, arsenic; nonvolatile residue, not more than ½ of 1 per cent) and for *assay* see U.S.P., p. 367.

SULFUR PRÆCIPITATUM—Precipitated Sulfur

(Sulfur Præc.)

Precipitated Sulfur, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of S.

Storage.—Preserve in well-closed containers.

Condensed Recipe (U.S.P. X).

Take 50 Gm. calcium oxide, slake and mix with 500 cc. of water, add 100 Gm. sifted sublimed sulfur, add 1000 cc of water and boil mixture for one hour. Decant clear liquid, filter the remainder and add to clear sulfur solution enough hydrochloric acid (16 per cent) to almost neutralize. Collect precipitate on strainer, and wash with water until free from calcium salts.

Summarized Description.

Fine yellow powder, responding to tests for sublimed sulfur. For details see U.S.P., p. 367.

For *tests for identity*, for *impurities* (arsenic, excess of acid or alkali) and for *assay* see U.S.P., p. 367.

Remarks.—Washed sulfur is sublimed sulfur from which the sulfurous and sulfuric acid have been removed by washing with a diluted solution of ammonia.

In subliming sulfur there is always sufficient air present to effect a slight oxidation of the sulfur, which means the production of sulfurous oxide, SO_2 and sulfuric oxide, SO_3, and these oxides pass over with the vaporized sulfur and are adsorbed upon solidification. Hence almost all sublimed sulfur contains traces of acid impurities. These impurities produce griping effect when contaminated sulfur is administered, and, accordingly, the removal of these traces of acid is advisable. This is accomplished by washing the sulfur with volatile alkali—ammonia water—this possessing the great advantage over the fixed alkalis (sodium hydroxide or potassium hydroxide) of being easily separated from the sulfur, simple exposure to air removing the last traces.

Precipitated sulfur is made by precipitating sulfur from its alkaline solution by the addition of hydrochloric acid, the equation of the two stages of the reaction being:

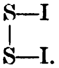
$$
\begin{array}{lllllll}
(a) & 3CaO & + & 6S & = & 2CaS_2 & + \; CaS_2O_3 \\
\text{Or} & 3CaO & + & 6S_2 & = & 2CaS_5 & + \; CaS_2O_3 \\
(b) & 2CaS_2 & + & CaS_2O_3 & + \; 6HCl & = & 3CaCl_2 + 6S + 3H_2O.
\end{array}
$$

The equations can be explained as follows: we prepare a solution of sulfur by chemically combining it with calcium oxide, whereby there is produced a soluble mixture of the polysulfides of sulfur, CaS_2 to CaS_5, and calcium thiosulfate, CaS_2O_3. This sulfur solution, a form of which is *solution of sulfurated lime* N.F. (see p. 213), is filtered, and to the clear liquid is added another clear liquid, hydrochloric acid, when a copious precipitate occurs, the acid seizing the calcium to form calcium chloride, going into solution, while the sulfur is precipitated. If, in the above reaction, sulfuric acid is used as a precipitant instead of hydrochloric acid, we obtain a precipitate consisting of sulfur contaminated with calcium sulfate. This body is known in commerce as *lac sulfur*, or milk of sulfur. The pharmacist must bear in mind that this does not represent the pharmacopœial precipitated sulfur, which one should specify by its official name in ordering. A simple test whereby to distinguish the official precipitated sulfur from the milk of sulfur is that the former, when burned on the end of a spatula, should yield no residue, whereas after burning the milk of sulfur there will remain a considerable quantity of calcium sulfate. All three official forms of sulfur enjoy considerable popularity as so-called "blood purifiers."

Dose.—(Of all three official forms of sulfur) 4 Gm. (60 grains).

Hydrogen Sulfide, H_2S, is the well-known gas of disagreeable odor, produced when ferrous sulfide or other sulfides is treated with a diluted acid. Its use in analytical chemistry is described in Part V. It should be borne in mind that it is poisonous when inhaled, as little as ½ of 1 per cent mixed in air having toxic effect.

Sulfuris Iodidum (U.S.P. VIII; N.F. V) is prepared by mixing sulfur and iodine together, after which they are heated in a flask until fusion is accomplished. The method is not satisfactory, since considerable iodine is lost by volatilization during the process of fusion. Prunier lessens this loss by first fusing the sulfur and then sprinkling the iodine in the fused mass. Iodized sulfur is an indefinite mixture, since it loses iodine on standing. It has been claimed to possess the formula S_2I_2, which can be explained by the following structural formula:



$$\begin{array}{l}S\text{—}I\\ |\\ S\text{—}I.\end{array}$$

In this it will be noticed that we have 2 atoms of bivalent sulfur; one bond of each is used in holding together its neighboring sulfur atom. Thus, each atom of sulfur has only one bond to which iodine is linked.

Carbonei Disulfidum (U.S.P. VIII) is made by passing the vapors of sulfur through carbon contained in a red-hot tube or cylinder.

Carbon disulfide is a heavy, mobile, inflammable liquid, with the offensive odor of rotten eggs. It is said to be odorless when absolutely pure, a happy condition never as yet attained by the writer, although he has often rectified the disulfide for analytic work.

This rectification can be performed by the ordinary process of distillation, with the one safeguard of preventing direct contact of the distilling flask with flame. For this reason it is even unadvisable to use a flame for heating the water on which the distilling flask rests. If a steam bath or an electric hot plate is not at hand, the distillation must be carried on by pouring heated water into the bath, rather than by directly heating the water. As carbon disulfide boils at 47° C., the occasional filling of the water baths with boiling water will very rapidly volatilize all the carbon disulfide. The chief use of carbon disulfide is as a solvent for India-rubber and was formerly official because of its use for this purpose in preparing mustard paper of the earlier Pharmacopœia.

NITROGEN

Symbol, N. Atomic weight, approximately 14

Nitrogen was discovered as a constituent of the air by Rutherford in 1772. The name nitrogen was coined from the two words *nitron*, niter, and *gennao*, I produce; investigation having shown that it was a constituent of niter or saltpetre. In 1919, E. E. Rutherford by bombarding nitrogen with the alpha rays of radium, disrupted the gas into hydrogen and helium.

Nitrogen is usually prepared on the small scale by heating ammonium nitrite (or, in practice a mixture of sodium nitrite and ammonium chloride), the equation of reaction being:

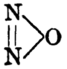
$$NH_4NO_2 + \text{heat} = N_2 + 2H_2O.$$

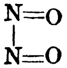
It is now being prepared by the distillation of liquefied air.

Nitrogen is a colorless, tasteless, odorless, and inert gas, which is of no pharmaceutic value. Its chief occurrence in uncombined state is in the atmosphere, of which it constitutes about 77 per cent by weight and 79 per cent by volume, and in which it does the inestimable service of diluting the very active constituent, oxygen. It has been proved that air is a mechanical mixture of nitrogen and oxygen, along with a small quantity of carbonic oxide, moisture, and traces of salts.

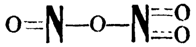
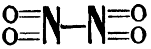
Nitrogen forms five chemical combinations with oxygen, and of these five oxides, only two follow the simple rules of valence.

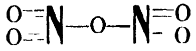
The graphic formulas of the five are supposed to be as follows:

Nitrogen monoxide, N_2O (Laughing-gas),

or $N\equiv N=O$

Nitrogen dioxide, N_2O_2,

$\begin{array}{l}N=O\\|\\N=O\end{array}$

Nitrogen trioxide, Nitrous oxide, N_2O_3, $O=N-O-N=O$

Nitrogen tetroxide, N_2O_4,

$O=N-O-N\begin{smallmatrix}=O\\=O\end{smallmatrix}$
or

$\begin{smallmatrix}O=\\O=\end{smallmatrix}N-N\begin{smallmatrix}=O\\=O\end{smallmatrix}$

Nitrogen pentoxide, Nitric oxide, N_2O_5,

$\begin{smallmatrix}O=\\O=\end{smallmatrix}N-O-N\begin{smallmatrix}=O\\-O\end{smallmatrix}$

Of these five oxides, two—nitrous oxide, N_2O_3, and nitric oxide, N_2O_5—will be considered in the next chapter among the acids. Of the other three, one is now official.

Nitrogen dioxide, N_2O_2, is incorrectly called nitric oxide, as that name more properly belongs to nitrogen pentoxide, N_2O_5, since that is the oxide from which nitric acid is derived.

Nitrogen dioxide is the colorless gas produced in a nitrometer when ethyl nitrite or other nitrites are treated with potassium iodide and sulfuric acid. It can be studied only in an inclosed apparatus like a nitrometer, for as soon as it comes in contact with the atmosphere it is converted into nitrogen tetroxide.

For this reason, while it is produced in oxidations with nitric acid (see manufacture of Solution of Ferric Sulfate (p. 570), it can never be detected when such reactions occur in the air, where, instead of the colorless nitrogen dioxide, the red-brown fumes of nitrogen tetroxide are evolved.

NITROGENII MONOXIDUM—Nitrogen Monoxide

(Nitrogen. Monoxid.—Nitrous Oxide)

N_2O. Molecular weight, 44.02

Nitrogen Monoxide contains not less than 95 per cent by volume of N_2O. For convenience it is usually supplied in compressed form in metallic cylinders.

Summarized Description.

Colorless gas; slight odor; sweetish taste; usually dispensed compressed in metallic cylinders; soluble in 1.5 volume of water at 20° C. For details see U.S.P., p. 242.

For *tests for identity* and for *impurities* (carbon dioxide, halogens, acids or alkalis, reducing substances, oxidizing substances) see U.S.P., p. 243.

Remarks.—This substance is called *laughing gas* and also, unfortunately, nitrous oxide, a synonym which should fall into disuse, since the term more properly belongs to nitrogen trioxide. It is made by heating ammonium nitrate, viz.:

$$NH_4NO_3 + \text{heat} = N_2O + 2H_2O.$$

It is a colorless gas of faint odor and sweetish taste and is used as an anesthetic, not only in dental practice but also in such operations as removing adenoid growths. It has lately been brought into prominence as an anesthetic by Crile who uses it in conjunction with the hypodermic administration of morphine and scopolamine and with a local anesthetic like novocain in performing "shockless operations."

Nitrogen tetroxide, N_2O_4, is of interest to us only because a product of oxidation with nitric acid mentioned above.

It is a heavy, red-brown, irritating vapor, and can be easily produced by pouring nitric acid on copper turnings.

It is claimed by some writers that N_2O_4 is colorless, and that the red-brown gas has the formula NO_2.

PHOSPHORUS

Symbol P. Atomic weight, approximately 31

The name phosphorus is derived from the two Greek words, *phos*, "light," and *pherein*, "to bring," hence the name light-carrier, designating the prominent characteristic of phosphorus, the term having been used before the discovery of phosphorus for other phosphorescent bodies.

Phosphorus was discovered by Brandt in 1669. This alchemist, in examining urine, placed some in a retort and subjected it to distillation. The residue in the retort, after the distillation, became charred, and the charcoal acted on the phosphates present, isolating free phosphorus, which appeared in the retort with its characteristic phosphorescence.

The manufacture of phosphorus from urine was in vogue for one hundred years, it being first prepared from bones by Scheele, in 1771, the element being discovered in bones by Gahn a few years earlier.

Phosphorus is never found in the free state in nature, as contact with the air causes a combination of it with the atmospheric oxygen.

It is found abundantly in the form of calcium phosphate in many minerals, such as *apatite*—calcium chlorophosphate and the *phosphate rock* of the southern Atlantic States. Calcium phosphate is also the main inorganic constituent of the bones, bone ash containing 86 per cent of that chemical.

Phosphorus is made from bone ash, there being several stages in the process. The bone ash is first treated with sulfuric acid, thus forming calcium sulfate and acid calcium phosphate, as shown in the following equation:

$$(a)\ Ca_3(PO_4)_2 + 2H_2SO_4 = 2CaSO_4 + CaH_4(PO_4)_2.$$

In passing, it might be mentioned that the acid calcium phosphate just cited is the constituent of the popular "*acid phosphates*," and similar preparations, such as the solution of phosphoric acid of the former editions of the National Formulary. In preparing phosphorus the acid phosphate obtained in the above reaction is then submitted to a high heat, whereby it loses water and is converted into calcium metaphosphate, as shown in the following equation:

$$(b)\ CaH_4(PO_4)_2 + \text{heat} = Ca(PO_3)_2 + 2H_2O.$$

This calcium metaphosphate is then heated with charcoal in a retort, and is decomposed into phosphorus and calcium pyrophosphate, as shown in the following equation:

$$(c)\ 2Ca(PO_3)_2 + 5C = P_2 + Ca_2P_2O_7 + 5CO.$$

A better yield of phosphorus can be obtained by using the larger proportion of carbon suggested in the following equation, thus getting calcium phosphate instead of calcium pyrophosphate:

$$(d)\ 3Ca(PO_3)_2 + 10C = P_4 + Ca_3(PO_4)_2 + 10CO.$$

In practice the reactions *b* and *c* are conducted together, and the isolated phosphorus is separated from the calcium pyrophosphate (or phosphate) by distillation; the distilled phosphorus being collected under warm water and run into molds while still fused.

Phosphorus is now being manufactured by heating calcium phosphate with charcoal and sand in the electric furnace, under an atmosphere of coal gas (Parker process).

Red phosphorus is prepared by heating the yellow variety to 300° C. in closed tubes, in an atmosphere of nitrogen. This product is a dark-red powder, perfectly stable in air, and comparatively nontoxic. Red phosphorus is largely used in place of yellow phosphorus in the manufacture of matches and the like, and its use has greatly lessened the dangers of this trade.

Metallic phosphorus is made by heating the red to 350° C. *in vacuo.* It appears in steel-like scales, and has no interest in pharmacy. Other forms of phosphorus have been recently described.

Phosphorus (U.S.P. X; N.F. VI) is the yellow allotropic form of the element and usually comes in commerce in cylindric sticks which must be kept under water or otherwise protected from the action of the atmosphere. This yellow phosphorus is as soft as wax, melts at 44° C., is soluble in absolute alcohol, ether, chloroform, and fixed oils. It is insoluble in water. Exposed to the air, yellow phosphorus catches fire spontaneously, emitting dense white fumes of phosphoric oxide, P_2O_5. This property renders it necessary to handle phosphorus with the utmost care, and in weighing same for pharmaceutic purposes it should always be done in water; *i. e.*, the stick of phosphorus should be cut under water contained in an evaporating dish, and weighed, not directly on the scale pan, but in a beaker glass containing water. That the weight of the beaker glass and the water should be previously determined goes without saying.

As mentioned above, the yellow phosphorus, even under water, emits a faint, whitish light. Some suppose this to be due to an evolution of minute quantities of phosphine, PH_3, and the immediate decomposition of same with the evolution of a microscopic flame: while others think it is due to formation and further oxidization of phosphorous anhydride.

Medical Properties.—Powerful nervous stimulant; a violent poison.

Dose.—0.6 mg. (1/100 grain).

Antidote.—Old (ozonized) oil of turpentine. Liquid petrolatum has been recently suggested as a phosphorus antidote. Ordinary fatty oils must never be used for this purpose.

Official Preparation.—Pills of phosphorus (U.S.P. X), each containing about 1/100 grain of phosphorus (p. 341).

N.F. V gave recipes for *oleum phosphoratum* or phosphorated oil, a 1 per cent solution of phosphorus in expressed oil of almond; *liquor phosphori* or Thompson's solution of phosphorus, containing 7/100 of 1 per cent of phosphorus in a mixture of glycerin and dehydrated alcohol, spirit of peppermint being used as a flavor. N.F. VI recognizes *elixir of phosphorus.* (See p. 230.)

CARBON

Symbol C. Atomic weight, approximately 12

The name of this element is derived from the word *carbo,* which was the Latin name for charcoal.

Carbon is found in the free form as diamond, graphite, and coal, while its combinations are very widely distributed. For example, all organic matter contains carbon. It is also found as carbonate in several well-known minerals; thus, marble and limestone are calcium carbonate, while dolomite is a mixture of calcium and magnesium carbonates.

Carbon, as such, is found in three allotropic forms, they being diamond, graphite, and charcoal. *Diamond* is the crystalline form of carbon, and is found in hard, transparent masses, possessing the specific gravity 3.5 to 3.6. The proof of its being carbon pure and simple is that when ignited in a stream of oxygen it is all consumed with the exception of a trace of ash (about $\frac{1}{10}$ of 1 per cent), forming nothing but carbon dioxide gas. Its formation from the other varieties of carbon has already been mentioned on p. 171.

Graphite is a gray-black, soft, amorphous solid, known to all as the so-called "lead" of the pencil. It has a specific gravity of about 2.25, and is of interest because of its resistance to heat. For this reason graphite is used for making crucibles—the so-called "black-lead crucibles." (See p. 98.)

Coal is the impure, noncrystalline form of carbon, and can be divided into two commercial varieties, *anthracite*, or hard coal, *bituminous*, or soft coal. Coal, on being heated in retorts, gives up its volatile portion, yielding illuminating gas, ammonia, and coal tar, while the residue is the commercial *coke*, which contains about 91 per cent carbon. The great value of coal and coke as a fuel has already been touched upon on p. 82.

Charcoals are more or less pure forms of amorphous carbon.

CARBO ACTIVATUS—Activated Charcoal

(Carbo Activat.)

The residue from the destructive distillation of various organic materials, treated to increase its adsorptive power.

Note.—When "Carbo Ligni" is prescribed, "Carbo Activatus" may be dispensed.

Storage.—Preserve in well-closed containers.

Summarized Description.

Black, odorless, tasteless powder, free from grit; burns with a nonluminous flame, leaving no more than 4 per cent of ash. For details see U.S.P., p. 107.

For *tests for identity*, for *impurities* (acid-soluble substances, chloride, sulfate, sulfide, cyanogen compounds, heavy metals) and for *adsorptive power*, see U.S.P., p. 107.

Remarks.—This form of charcoal replaces Carbo Ligni of U.S.P. X. It represents a carbon from any source, standardized for its adsorption capacity. In the official monograph three tests for adsorption power are provided: (*a*) adsorption of strychnine sulfate; (*b*) adsorption of methylthionine chloride; (*c*) adsorption of sodium sulfide. For details see U.S.P. XI.

High adsorptive charcoals were found essential in gas masks during the World War. Thousands of experiments were performed by the Chemical Warfare Service of this country and all types of charcoal were studied. Among these were special types of both vegetable and animal charcoals, such as that from coconut shells, bones, blood, and even the dried carbonized residue from sulfite waste liquor from the pulping of wood for paper. The modern types are activated; that is charcoal undergoes some type of chemical treatment and many of these are kept trade secrets. At the present time most of the activated charcoal is used for large-scale decolorizing processes (see p. 162). Modern clinical experience has however shown the value of adsorptive agents on medication.

Dose.—1 Gm. (15 grains).

Carbo Ligni (U.S.P. X) or *wood charcoal* has been replaced by *Carbo Activatus* described above.

Carbo Animalis (U.S.P. VIII), commercially called *bone black*, is prepared by placing dried bones in a cast-iron retort and carbonizing (during the process a liquid distils over which is called *bone oil*), and the residue in the retort is then removed and reduced to powder. Animal charcoal contains the carbon from the organic matter of the bones plus all the bone ash, and it therefore contains a large amount of calcium phosphate. Animal charcoal is used as a decolorizer, as explained on p. 162, and the presence of calcium phosphate therein renders its use inadvisable in removing color from liquids containing acids as calcium phosphate will dissolve therein. Preferable therefore is:

Carbo Animalis Purificatus (N.F. VI) which is made by digesting animal charcoal with hydrochloric acid on a sand bath for a period of eight hours, and, after straining the liquid, returning the charcoal to the vessel. The operation is repeated with a second amount of hydrochloric acid, and the digestion continued for two hours. Finally, the acid is drained off, the charcoal freed from all traces of acid by washing with water, and the product dried. The acid effects the solution of the bone ash by converting it into soluble acid calcium phosphate, described in the manufacture of phosphorus (p. 432). Purified animal charcoal is an excellent decolorizer, and should always be used by the pharmacist in preference to the crude product. Knecht claims that animal charcoal contains nitrogen and that its decolorizing power is directly proportional to its nitrogen content.

The removing of color by means of purified animal charcoal is performed by macerating the liquid with the charcoal for several hours, and finally filtering. It is well to remember that animal charcoal not only absorbs the color from a solution, but also absorbs some active plant principles, such as alkaloids and glucosides. Therefore, care should be taken to avoid the loss of active ingredients by too long contact with the charcoal.

Lamp black is carbon produced by burning petroleum, or natural gas in a limited amount of air, and collecting the "soot" thus produced.

CARBONEI DIOXIDUM—Carbon Dioxide

(Carbon. Diox.—Carbonic Acid Gas)

CO_2. Molecular weight, 44.00

Carbon Dioxide contains not less than 99 per cent by volume of CO_2. For convenience it is usually supplied in compressed form in metallic cylinders.

Summarized Description.

Heavy, odorless, colorless gas; faintly acid taste when moist. Soluble in an equal volume of water at 25° C. For details see U.S.P., p. 108.

For *tests for identity*, for *impurities* (acid, sulfur dioxide, phosphine, hydrogen sulfide, organic reducers and carbon monoxide) and for *assay*, see U.S.P., p. 108.

Remarks.—Carbon dioxide, CO_2, is obtained: (*a*) when a carbonate is treated with the appropriate acid, (*b*) when limestone is calcined (p. 521), (*c*) during the process of fermentation. That for medicinal purposes is usually produced by the first-named process. It was introduced into U.S.P. XI because of its large use for producing local anesthesia by freezing (see Rhigolene, p. 641). Its solution in water produces the well-known carbonated beverages. It is a gas that on subjection to cold and pressure is converted into a liquid. This liquid upon sudden ejection from its steel container will partially evaporate leaving a solid residue (CO_2 snow or *dry ice*) which is now produced in enormous quantities for use as a freezing agent. See *Refrigeration*, p. 90.

BORON

Symbol, B. Atomic weight, approximately 11

The word boron comes from *boraq*, which was the Arabic name for borax. The element was first isolated by Gay-Lussac and Thenard in 1808.

Boron occurs in nature in the form of boric acid, sodium borate, and boracite, the latter being a magnesium borate. It is found in two allotropic forms, crystalline and amorphous. Its compounds with hydrogen and oxygen yield several acids, such as boric, metaboric, and pyroboric acids. Boron is not official, but it is found in two official bodies—boric acid and borax.

ACIDUM BORICUM—Boric Acid

H_3BO_3. Molecular weight, 61.84

Boric Acid, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of H_3BO_3.

Storage.—Preserve boric acid in well-closed containers.

Summarized Description.

Colorless scales, triclinic crystals or white bulky powder; unctuous to touch; odorless; faintly bitter; soluble in 18 parts of water and 18 parts of alcohol. Heated it first forms metaboric acid and then fuses to tetraboric acid and finally to boron trioxide. For details see U.S.P., p. 18.

For *tests for identity*, for *impurities* (heavy metals, arsenic, insoluble substances) and for *assay* see U.S.P., p. 18.

Remarks.—The formula of this compound, frequently called *boracic acid*, has already been discussed (p. 395), so here it is only necessary to emphasize the fact that boric acid is the only true official ortho-acid.

Boric acid is found in the free form in lagoons in volcanic regions of Tuscany, the water being evaporated with the aid of the jets of steam emitted from the volcanic soil.

It is now made in large quantities in this country from native borax (p. 481), by treating it with hydrochloric acid, the equation being:

$$Na_2B_4O_7.10H_2O + 2HCl = 2NaCl + 4H_3BO_3 + 5H_2O.$$

Boric acid is found in the form of crystalline micaceous scales, which possess a peculiar unctuous feeling. Boric acid is volatile, but more freely, however, in the vapor of water than if heated by itself. Boric acid is now popular in the form of an impalpable powder, and the preparation of this caused considerable annoyance on account of the slipperiness of the crystals, until it was found that trituration of boric acid in a warmed mortar or mill brings the desired results.

The two tests of boric acid are, first, the fact that an alcoholic solution burns with a flame enveloped with a green mantle, and, secondly, its property of changing yellow turmeric paper to a reddish brown.

Boric acid is a useful antiseptic and is largely used in domestic practice for this purpose. It is a constituent of *glycerite of boroglycerin* and of *ointment of boric acid*, as well as in the *antiseptic solution* of the National Formulary.

Dose.—500 mg. (8 grains).

Liquor Acidi Borici (N.F. VI), or *Solution of Boric Acid*, has been introduced into the Formulary in response to a demand for a standard *saturated solution of boric acid*. It is made by dissolving 50 Gm. of the acid in 350 cc. of distilled water and then adding enough cold distilled water to make 1000 cc. It is to be filtered, if necessary. For further details, the Formulary should be consulted. This solution is apt to develop growths (*Torula* species) if carelessly stored, hence the importance in preparing it with recently boiled distilled water and of preserving it in sterile containers. While it is commonly considered harmless as a mouth wash for babies, several cases of wholesale poisonings in hospitals have been reported where the saturated solution has been accidentally administered to infants in place of water.

SILICON

Symbol, Si. Atomic weight, approximately 28

The word silicon is derived from *silica*, or sand, which in turn is derived from the Latin *silex*, which means flint. The element was isolated by Berzelius in 1823. Silicon is the most abundant element on the earth's surface.

Thus, quartz, sand, opal, agate, and infusorial earth are more or less pure forms of silica. While this is usually assigned the formula SiO_2, Martin believes its minimum molecular formula is Si_6O_{12}.

Silica ware represent chemical utensils made of fused quartz (see p. 99). Crucibles and evaporating dishes made of this material are very durable. Recent manufacturing developments now permit the production of silica reaction vessels as large as 108-gallon capacity.

Silicon is another element appearing in two allotropic forms, crystalline and amorphous. None of the forms of silicon is of sufficient pharmaceutic interest to merit more than passing notice. Silicon, as shown on p. 391, yields one oxide, SiO_2; one form of which, *purified siliceous earth,* is official. The hypothetic combinations of this, with water, are silicic acids, H_2SiO_3, and H_4SiO_4, and the salts of these acids are the ordinary silicates. Silicates of complex formulas, such as *orthoclas,* $K_2AlSi_6O_{16}$, are known.

Glass is a combination of the silicates of sodium or potassium with lead or calcium.

The test for soluble silicates is that they yield with acids a white gelatinous precipitate of orthosilicic acid, H_4SiO_4.

The silicates other than those of the alkalis are insoluble in all acids, even the strongest, except hydrofluoric acid.

In order to obtain these silicates in soluble form it is necessary to fuse them with a mixture of sodium and potassium carbonates, whereby silicates of sodium and potassium are formed.

TERRA SILICEA PURIFICATA—Purified Siliceous Earth

(Ter. Sil. Purif.—Purified Kieselguhr, Purified Infusorial Earth)

Purified Siliceous Earth is a form of silica (SiO_2), consisting of the frustules and fragments of diatoms, purified by boiling with diluted hydrochloric acid, washing, and calcining. It contains not more than 10 per cent of water.

Storage.—Preserve in well-closed containers.

Summarized Description.

Very bulky fine powder; white, light gray or pale buff; absorbs 4 times its weight of water; insoluble in water. For details see U.S.P., p. 382.

For *tests for identity,* and for *impurities* (moisture, organic matter, soluble iron, carbonate, sulfate), see U.S.P.

Remarks.—This official substance represents that form of infusorial earth (diatoms) known as *Kieselguhr.* It is now used as a filtering agent and is recommended for this purpose in the pharmacopœial monograph on aromatic waters. Kaolin, aluminum silicate, is discussed on p. 549 and sodium silicate on p. 496.

BIBLIOGRAPHY

Hydrogen.—(History) Hackh, A.J.P., 90, 1918, 569; Edit., Jl. Soc. Ch. Ind., 50, 1931, 837. (Technical manufacture) Sander, Zt. angew. Ch., 25, 1913, 2401; Barnitz, A.J.P., 88, 1916, 264 and 89, 1917, 313; Sadtler, *ibid.*, 95, 1923, 278. Anon., Jl. Soc. Ch. Ind., 44, 1925, 131; Knowles, *ibid.*, 45, 1926, 121 and 137; Thorpe, *ibid.*, 48, 1929, 281; Anon., *ibid.*, 51, 1932, 355. (Atomic and isotropic hydrogen) Langmuir, Jl. Ind. Eng. Ch., 19, 1927, 667 and Jl. Soc. Ch. Ind., 47, 1928, 134; Urey, Murphy and Brickwedde, Science, 78, 1933, 566; Leboucq, Jl. ph. et. Ch. [8], 10, 1929, 549. (Properties) Bancroft, Science, 66, 1927, 173.

Helium.—(History) Weaver, Jl. Ind. Eng. Ch., 11, 1919, 682; Lockyer, Ch. News, 19, 1869, 158 and 56, 1887, 267; Ramsay, *ibid.*, 71, 1895, 151 and 72, 1896, 87; Moore, Jl. Frank. Inst., 191, 1921, 145. (Production) Cottrell, Jl. Ind. Eng. Ch., 11, 1919, 148; Moore, C.A., 17, 1923, 1111; Taylor, Jl. Soc. Ch. Ind., 48, 1929, 369T; Anon., Jl. Ind. Eng.

Ch., 22, 1930, 1017 and 24, 1932, 1435; Langton, Jl. Soc. Ch. Ind., 50, 1931, 472. (Properties) Keesom, C.A., 23, 1929, 1045; Snyder and Bottoms, Jl. Ind. Eng. Ch., 22, 1930, 1189; Burgess, Jl. Frank. Inst., 211, 1931, 653; McLennam and co-workers, Science, 75, June 3, 1932, Supp. 8.

Oxygen.—(History) Hackh, A.J.P., 90, 1918, 569; Anon., Jl. Frank. Inst., 195, 1923, 138. (Production) Foregger, Am. Dr., 48, 1906, 158; Linde, Eng. Pat., 14111, 1902; Kassner, C.A., 8, 1914, 1332; Anon., C.A., 8, 1914, 266; Sadtler, A.J.P., 95, 1923, 270; Fuldman, Jl. Soc. Ch. Ind., 43, 1924, 440; Kassner, C.A., 19, 1925, 2391; Sweeny and co-workers, Jl. Ind. Eng. Ch., 22, 1930, 716. (Therapeutics) Ellis, Ch. and Dr., 92, 1920, 748.

Ozone.—(History) Oesper, Jl. Ch. Ed., 6, 1929, 679. (Source) Kershaw, Elect. World, 58, 1912, 1192; Sawyer and others, Jl. A.M.A., 61, 1913, 1013. (Properties) Harrison, Jl. Frank. Inst., 209, 1930, 433. (Assay in air) Hatcher and Arny, A.J.P., 72, 1900, 423.

Distilled Water.—(Preparation) Bourdas and Touplain, C.A., 20, 1926, 1929. (Cryptogams in) Julliet, Bull. pharm. Sudest, 18, 1913, 603. (Sterilization) Cook and Gershenfeld, Jl. A.Ph.A., 8, 1919, 116.

Heavy Water.—Lewis, also Washburn, Science, 78, Sept. 1, 1933, Suppl. 6.

Hydrogen Dioxide.—(History) Brewer, Dr. Circ., 56, 1912, 609. (Structure) Anon., Pharm. Era, 47, 1914, 155; Geib and Harteck, B., 65, 1932, 1551. (Properties) Brühl, B., 28, 1895, 2857; Maass and co-workers, Jl. Am. Ch. Soc., 42, 1920, 2548 and 2569; 50, 1928, 1120 and 51, 1929, 674. (Manufacture) Kirkpatrick, Jl. Am. Ch. Soc., 48, 1926, 3019; Zotos, Ch. Zt., 54, 1930, 665 and 686. (Properties and uses) Agde and Alberti, Jl. Soc. Ch. Ind., 45, 1926, 821; Anon., Jl. Ind. Eng. Ch., News. Ed., 8, Apr. 20, 1930, 11. (Perhydrol and Hyperol) Erdenbrecher, Jl. Soc. Ch. Ind., 43, 1924, 710B; Booer, *ibid.*, 44, 1925, 1137.

Solution of Hydrogen Dioxide.—(Manufacture), Anon., Dr. Circ., 15, 1871, 125. Arny, Dr. Circ., 58, 1914, 277; Doerner, Ch. Met. Eng., 26, 1922, 1111. (Antiseptic Value) Benedict, Am. Dr., 16, 1887, 207. (Preservation) LaWall, A.J.P., 78, 1906, 582; Clover, *ibid.*, 85, 1913, 538; Poetschke, Jl. Ind. Eng. Ch., 14, 1922, 181; Tellera, C.A., 24, 1930, 205. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1156.

Chlorine.—(History) Chattaway, Ch. News, 101, 1910, 25 and 73; Pearson, Jl. Soc. Ch. Ind., 43, 1924, 247; Pritchard, Jl. Soc. Ch. Ind., 47, 1933, 57; Dobbin, Ch. and Dr., 113, 1930; 406 and 115, 1931, 400. (Manufacture) Askenasy, Ch. Zt., 35, 1911, 609; Weldon, Ch. News, 20, 1869, 109; Deacon, *ibid.*, 22, 1870, 157; Chaleyer, Jl. Soc. Ch. Ind., 39, 1920, 105A; Weldon, Jl. Soc. Ch. Ind., 2, 1882, 39. (Bleaching action) Popper, Am. Dr., 15, 1886, 55; Weiss, C.A., 25, 1931, 2044. (Liquid chlorine) Kingsley, Ph. Era., 62, June 5, 1926, 27; Freund, Jl. Soc. Ch. Ind., 47, 1928, 225; Wells and co-workers, *ibid.*, 45, 1926, 486B.

Chlorine Water.—(Preservation) Spenzer, Am. Dr., 17, 1888, 152.

Compound Solution of Chlorine.—W., A.J.P., 42, 1870, 207; Gooch and Kreider, Ch. News, 70, 1894, 155.

Chlorinated Lime.—(History) Anon., Jl. Soc. Ch. Ind., 42, 1923, 384; Edit. Jl. Soc. Ch. Ind., 45, 1926, 136; Szathmary, C.A., 25, 1931, 5319. (Chemical composition). Taylor, Jl. Ch. Soc., 97, 1910, 2541; Taylor and Bostock, *ibid.*, 101, 1912, 444; Kraut, A., 214, 1882, 354 and 221, 1883, 108; Ochi, Jl. Soc. Ch. Ind., 42, 1923, 603A; Urano, Jl. Soc. Ch. Ind., 45, 1926, 485B; Ochi, *ibid.*, 45, 1926, 438B; Neumann and co-workers, *ibid.*, 45, 1926, 190B; C.A., 24, 1930, 1592; *ibid.*, 24, 1930, 5655; O'Connor, *ibid.*, 22, 1928, 738; Kingsett, *ibid.*, 22, 1928, 2034. (Manufacture) Lunge and Naef, A., 219, 1883, 129; Thomson, A.J.P., 13, 1841, 206; Conroy, Jl. Soc. Ch. Ind., 25, 1906, 1011; Richardson and co-workers, Jl. Soc. Ch. Ind., 45, 1926, 125B; Angel, C.A., 23, 1929, 1476; Carughi and Paoloni, *ibid.*, 26, 1932, 2827. (As water purifier) Thresh, A.Ph.A., 57, 1909, 235; ("Active chlorine" content) Anon., Ph. Zt., 68, 1923, 738; Eckert, *ibid.*, 71, 1926, 1607; Arny, Am. Dr., 78, Dec., 1928, 80. (Deterioration) McDonnell and Hart, Jl. Soc. Ch. Ind., 45, 1926, 404B; Aguilar, *ibid.*, 51, 1932, 382B.

H. T. H.—(Manufacture) MacMullin and Guyer, U. S. Pat. 1,754,473. (Composition) Melkan, C.A., 25, 1931, 1634.

Labarraque's Solution.—(History) Anon., Am. Dr., 15, 1886, 180; Langenhan and Irish, Jl. A.Ph.A., 9, 1920, 497; Davis and Langenhan, *ibid.*, 13, 1924, 32. (Manufacture) Elvove, A.J.P., 82, 1910, 161; Kolkin, Jl. Soc. Ch. Ind., 51, 1932, 381B. (Composition) Arny and Wagner, A.J.P., 76, 1904, 258; Arny and Dawson, A.Ph.A., 56, 1908, 841. (Deterioration) Wells, A.J.P., 98, 1926, 404; Kürschner, Ph. Zt., 76, 1931, 184; Arny and co-workers, Jl. A.Ph.A., 20, 1932, 1155. (Preservation) Cullen and Hubbard, C.A., 13, 1919, 2105.

Dakin's Solution.—(History) Dakin, Jl. A.M.A., 66, 1916, 430. (Manufacture) Carrel and Dehelly, Am. Dr., 65, 1917, 97; Griffith, Proc. P.P.A., 40, 1917, 237; Ornstein, A.J.P., 87, 1917, 547; Kelly and Kranz, Jl. A.Ph.A., 12, 1923, 112; Davis and

Langenhan, *ibid.*, 13, 1924, 127, 219 and 321; Harrison, Jl. A.Ph.A., 13, 1924, 902. (Deterioration) Krantz and Vidal, Jl. A.Ph.A., 15, 1926, 359.

Bromine.—(History) Sharp, Ph. Jl., 87, 1912, 128; Chattaway, Ch. News, 99, 1909, 205. Anon., Ch. and Dr., 105, 1926, 363. (Sources) Berglund, Am. Dr., 15, 1886, 53; Tyler and Clinton, Bureau Mines, Inf. Circ., 6387, 1930, 1–26; DeLong, Jl. Ind. Eng. Ch., 18, 1926, 425. (Manufacture) Seebohm, A.Ph.A., 33, 1885, 223; Dow, Ch. Met. Eng., 21, 1919, 452; Huttner, Z. angew. Ch., 35, 1922, 431. (Production) Moreschi, C.A., 20, 1926, 3540; Dow, Jl. Ind. Eng. Ch., 22, 1930, 113; Kaltenbach, Jl. Soc. Ch. Ind., 50, 1931, 537B. (Properties) Bonzat and Leluan, Jl. Frank. Inst., 197, 1924, 666. (Shipping precautions) Dunn, C.A., 10, 1917, 1548.

Iodine.—(History) Chattaway, Ch. News, 99, 1909, 193; Becker, Schw. Wsch. f. Ch. u. Ph., 50, 1912, 586; Sharp, Ph. Jl., 91, 1913, 98; Edit. Jl. Soc. Ch. Ind., 48, 1929, 232 and 50, 1931, 316. (Sources) Bain and Mulliken, C.A., 18, 1924, 884 and 19, 1925, 371; Reith, *ibid.*, 24, 1930, 1817; Tyler and Clinton, *ibid.*, 25, 1931, 384; Anon., Ph. Jl., 127, 1931, 476, Anon., Science, 77, Feb. 10, 1933, Supp. 8. (Manufacture) Delaunay and others, A.J.P., 18, 1847, 324; Anon., Am. Dr., 19, 1890, 25; Anon., Ch. and Dr., 71, 1907, 555; Porteus, A.Ph.A., 6, 1857, 110; Newton, Jl. Soc. Ch. Ind., 22, 1903, 469; Doherty, C.A., 13, 1919, 364; Faust, Jl. Ind. Eng. Ch., 18, 1926, 808; Anon., Ch. and Dr., 108, 1928, 197; Averkiev and Komareckyj, C.A., 23, 1929, 4025 and 5014. (Sublimation) Koehler, C.h Zt., 39, 1915, 122. (Medical action) Erlenmeyer and Stein, Nat. Dr., 39, 1909, 280; Niece, Dr. Circ., 58, 1914, 206; Anon., Prescriber, 8, 1914, 1909; Maben and White, Ch. and Dr., 86, 1915, 144; Bircher, C.A., 17, 1923, 436; Prinz, "Iodine Therapy," 1931; LaWall and Tice, Jl. A.Ph.A., 21, 1932, 122; Gershenfeld and Miller, *ibid.*, 21, 1932, 894. (Incompatibility) Reutter, C.A., 9, 1915, 1664. (Properties) Kruss and Thiele, Zt. anorg. Ch., 7, 1894, 52; Lachmann, Jl. Am. Ch. Soc., 25, 1903, 50; Griffith, A.J.P., 102, 1930, 179: Getman, Jl. Am. Ch. Soc., 50, 1928, 2883; Delépine and Arquet, C.A., 22, 1928, 668; Groh and Papp., *ibid.*, 24, 1930, 4710; Lanza, *ibid.*, 25, 1931, 3133 and 26, 1932, 892. (Solubility) Davis, Dr. Circ., 54, 1910, 584; Grimbert, Malmy and Poirot, Jl ph. ch., 29, 1924, 5; Murray, Jl. Ch. Soc., 127, 1925, 1288; Gorbatscheff and Winograda, C.A., 21, 1927, 3148; Turner, Jl. Am. Ch. Soc., 52, 1930, 2768; Pictet and Vogel, C.A., 24, 1930, 345; Hofmann, *ibid.*, 26, 1932, 3449. (Reactions) Fordos and Gélis, Ann. de chim. et de phys., [3], 6, 1842, 484; Berczeller, Ji. Soc. Ch. Ind., 42 (1923) 322 A.

Tincture of Iodine.—Duhamel, A.J.P., 6, 1834, 114; Wetterstroem, Proc. Ohio Ph. A., 1908, 52; Courtot, D. A., Ap. Zt., 31, 1911, 32; LaWall, A.Ph.A., 55, 1907, 156; Doste, C.A., 8, 1914, 3345; Shaw and Cofman, Ph. Jl., 110, 1923, 452; Stephenson, Ph. Jl., 109, 1922, 610; Copley, Jl. A.Ph.A., 13, 1924, 806; Carter, Jl. Ind. Eng. Ch., 18, 1926, 827; Thomann, Schw. Apoth. Zt., 65, 1927, 277, 289, 301 and 325; Bohrisch, Apoth. Zt., 43, 1928, 436; Veraart and Drenth, C.A., 27, 1933, 161.

Colorless Tincture of Iodine—Dickinson, A.Ph.A., 44, 1896, 455; Mendelsohn, Jl. A Ph.A., 13, 1924, 223; Rang, Master's Dissertation, Univ. Wis., 1925; Kunz-Krause, Arch. d. Pharm., 261, 1923, 173.

Colloidal Iodine.—Chandler, Nat. Dr., 59, 1929, 381; Myiri and Dubois, Jl. A.Ph.A., 20, 1931, 546; Bennett, A.J.P., 103, 1931, 51; Hopkins, Ph. Jl., 126, 1931, 538; Starkman, Can. Ph. Jl., 66, 1932, 186.

Sulphur.—(History) Hackh, A.J.P., 90, 1918, 485. (Extraction) Washington, The Man Farthest Down, 1912, 201; Frasch, Jl. Ind. Eng. Ch., 4, 1912, 136. Jones, Ch. and Dr., 93, 1920, 995; Davis, Jl. Ind. Eng. Ch., 15, 1923, 14; Lundy, Chem. Met. Eng , 32, 1925, 917; Claudin, C.A., 26, 1932, 2557; Taylor, Jl. Ind. Eng. Ch., 24, 1932, 1116. (Sources) Ridgway, Bureau of Mines Inf. Circ., 6329, 1930, 1–55; Anon., Jl. Soc. Ch. Ind., 50, 1931, 594; Anon., Jl. Ind. Eng. Ch., 24, 1932, 374. (Allotropic forms) Cohen, C.A., 6, 1912, 339; Pruner and Schupp, Zt. Phys. Ch., 68, 1909, 157; Stafford, Zt. phys. Ch., 77, 1911, 66; Citen, C.A., 9, 1915, 6; Kellas, Ch. News, 118, 1919, 47; Huerre, Jl. ph. Ch., 28, 1923, 223; Morgan, Jl. Soc. Ch. Ind., 44, 1925, 82. (Solubility) Henville, Analyst, 55, 1930, 385. (Colloidal forms) Sobrero and Sehni, A.Ph.A., 57, 1909, 241; Bucciardi, C.A., 23, 1929, 2212; Rossi and Marescotti, *ibid.*, 23, 1929, 5384. (Pharmacology) Wild and Grier, Merck's Rep., 20, 1911, 61.

Precipitated Sulphur.—(Composition and manufacture) Schweitzer, Ph. Jl., 2, 1843, 517. (Manufacture) Reed, A.Ph.A., 45, 1897, 240; Sayre, Dr. Circ., 41, 1897, 318.

Vleminckx's Solution.—Mayer, Dr. Circ., 58, 1914, 396.

Lac Sulphur.—Attfield, Ph. Jl., [2], 10, 1869, 472.

Sulphur Iodide.—Prunier, Jl. de ph., [6], 9, 1899, 421; Linebarger, Am. Ch. Jl., 17, 1895, 33; Amadori, C.A., 16, 1921, 3576.

Carbon Disulphide.—(Manufacture) Deiss, A.J.P., 52, 1880, 199; Anon., Dr. Circ., 37, 1893, 83; Rabe, Jl. Soc. Ch. Ind., 45, 1926, 874B.

Nitrogen.—(History) Chaptal-Woodhouse, Elements of Chemistry, 1, 1807, 12;

Lavoisier-Kerr, Chemistry, 1806, 81; Hackh., A.J.P., 90, 1918, 569. (Atomic weight) Moles, C. A., 22, 1928, 517. (Disruption) Rutherford, C.A., 13, 1919, 2481 and 14, 1920, 3570.

Nitrogen Monoxide.—(History) Harrison, Ph. Jl., [2], 11, 1870, 704. (Manufacture) Warner, Jl. A.M.A., 65, 1915, 1973. (Structure) Noyes, Jl. Am. Ch. Soc., 52, 1930, 4298; Stuart and Volkmann, C.A., 26, 1932, 4512. (Medical use) Teeter, Lancet, 112, 1914, 634; Baldwin, Ph. Jl., 99, 1917, 125; Baskerville and Stevenson, Jl. Ind. Eng. Ch., 3, 1911, 579; Crile, Jl. A.M.A., 67, 1916, 1830; Henderson and Lucas, C.A., 24, 1930, 4582.

Phosphorus.—(History) Anon., Ph. Jl., [3], 25, 1895, 937; Peters, Ch. Zt., 26, 1902, 1190 and Ph. Jl., 104, 1920, 369; Palet, C.A., 12, 1918, 1017; Hackh, A.J.P., 90, 1918, 567; Speter, Jl. Soc. Ch. Ind., 49, 1930, 381. (Manufacture) Readman, Jl. Soc. Ch. Ind., 9, 1890, 163 and 472. (Phosphorescence and coating) Thorpe, Ph. Jl., [3], 20, 1890, 845; Germez, Jl. Am. Soc., 33, 1911, 175; Stock, Schrader and Stamm, B., 45, 1912, 1514; Bloch, C.A., 3, 1909, 399; Bec, C.A., 13, 1919, 3078; Rayleigh, C.A., 15, 1921, 3938; Corrigan, Ch. News, 122, 1921, 25. (Allotropic forms) Cohen, Jl. Am. Ch. Soc., 33, 1911, 175; Bridgman, Jl. Am. Ch. Soc., 36, 1914, 1344. (Antidote) Atkinson, Am. Dr., 71, May, 1923, 43.

Acid Phosphate.—Pepper, A.J.P., 52, 1880, 481.

Safety Matches.—Norton, Jl. Ind. Eng. Ch., 4, 1912, 53.

Carbon.—(History) Hackh, A.J.P., 90, 1918, 486. (Occurrence) Stevenson, C.A., 6, 1912, 729; Derby, C.A., 6, 1912, 727 and 3384; Geare, Merck's Rep., 24, 1915, 3, (Melting point) Alterthum and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 629B.

Diamonds.—(Source) Garrison, Jl. Frank. Inst., 211, 1931, 197. (Artificial) Ramsey, Jl. Ch. Soc., 101, 1912, 477.

Graphite.—(Source and properties) Seton, Jl. Soc. Ch. Ind., 49, 1930, 493. (Artificial) Acheson, Jl. Ind. Eng. Ch., 4, 1912, 62; Slater, Jl. Soc. Ch. Ind., 44, 1925, 501T.; Jl. Ind. Eng. Ch., 23, 1931, 719. (Graphite pencils) Mitchell, Jl. Soc. Ch. Ind., 38 (1919) 383T.

Lamp Black.—Butler, C.A., 6, 1912, 799; Alcock, Ch. and Dr., 75, 1909, 443; Perrott and Thiessen, Jl. Ind. Eng. Ch., 12, 1920, 324. Grove-Palmer, Jl. Soc. Ch. Ind., 48, 1929, 60; Weigand, Jl. Ind. Eng. Ch., 23, 1931, 178.

Animal Charcoal.—Knecht, A.Ph.A., 56, 1908, 271.

Wood Charcoal.—Havenhill, Dr. Circ., 58, 1914, 260; Piutti and Magli, C.A., 3, 1909, 10; Hommell, Pr. Dr., 49, May, 1931, 15; Schofield, C.A., 26, 1932, 4737.

Charcoals.—(As absorbents) Stenhouse, Ph. Jl., 16, 1851, 363; Rosenberg, Ph. Zt., 66, 1921, 723; Calvert, Jl. A.Ph.A., 11, 1922, 798; Anon., Jl. Ind. Eng. Chem., 11, 1919, 420; Merck, Ph. Zt., 69, 1924, 523; Dingemanse and Laquer, Jl. Soc. Ch. Ind., 44, 1925, 1010B; Henglein and Grzenkovski, *ibid.*, 45, 1926, 143B.; Brindle, Ph. Jl., 121, 1928, 84; Dubinin, C.A., 24, 1930, 282; Goiffon, *ibid.*, 24, 1930, 3563. (As decolorizers) Helch, C.A., 9, 1915, 1527; Joachimoglu, Pharm. Weekbl., 54, 1917, 1173; Zerban, Yearbook A.Ph.A., 7, 1918, 349; Van Os, C.A., 14, 1920, 2841; Bock, Jl. Am. Ch. Soc., 42, 1920, 1564; Rosenberg, Ph. Zt., 66, 1921, 724; Koenig, C.A., 17, 1923, 2473; Horne, Jl. Ind. Eng. Ch., 16, 1924, 670; Tanner, *ibid.*, 17, 1925, 1191; Sasaki, C.A., 23, 1929, 4120; Strachan, Jl. Soc. Ch. Ind., 47, 1928, 1203.

Carbo Activatus.—Rosin, Beal and Szalkowski, Jl. A.Ph.A., 24, 1935, 634.

Carbon Dioxide.—(History) Anon., Jl. Soc. Ch. Ind., 47, 1928, 739; Anon., *ibid.*, 48, 1929, 341. (Properties) Cooper and Maass, C.A., 25, 1931, 3212; Card, Drug. Bull., 51, June, 1929, 30.

Solid CO_2.—Howe, Jl. Ind. Eng. Ch., 20, 1928, 1091; Goosmann, C.A., 23, 1929, 2512 and 25, 1931, 1952 and 5251; Thurston, Jl. Soc. Ch. Ind., 48, 1929, 95B and 323B; Killeffer, Jl. Ind. Eng. Ch., 22, 1930, 1087.

Boron.—Hampe, A., 183, 1876, 75; Biltz, B., 43, 1910; 297; Gay-Lussac, Recherches phys. chim., 1808, through Gmelin-Kraut, 13, 1911, 386; Davies, Ph. Jl., [3], 11, 1880, 451. (Manufacture and properties) Wöhler and Deville, A.J.P., 29, 1857, 339.

Boric Acid.—(Occurrence) Frank, C.A., 1, 1907, 1045; Funaioli, Yearbook A.Ph.A., 7, 1918, 349; Anon., Jl. Soc. Ch. Ind., 42, 1923, 1022; Conti, Jl. Soc. Ch. Ind., 43, 1924, 739 and 44, 1925, 343T. (Volatility) Anschütz and Riepenkröger, B., 58, 1925, 1734. (Toxicity) McNally and Rust, Jl. A.M.A., 90, 1928, 382.

Silicon.—Berzelius, Pogg. Ann., 1, 1823, 165, through Meyer-McGowan, 1906, 422; Robinson and Smith, C.A., 20, 1926, 3264; Viehoever, A.J.P., 104, 1932, 107.

Silica.—(Structure) Martin, C.A., 9, 1915, 2848 and 2888. (Utensils) Browne Ph. Jl., 99, 1917, 86; Thomson, Jl. Frank. Inst., 200, 1925, 313; Anon., *ibid.*, 200, 1925, 132; Berry, Jl. Soc. Ch. Ind., 45, 1926, 35; Moore, *ibid.*, 50, 1931, 671.

Infusorial Earth.—Phalen, C.A., 3, 1909, 231; Boeck, C.A., 8, 1914, 1332; Goodwin, C.A., 15, 1921, 928; Anon., Jl. Ind. Eng. Ch., 20, 1928, 1195; Eardley-Wilmot, Jl. Soc. Ch. Ind., 48, 1929, 94; Hendley, Ph. Jl., 125, 1930, 97; *ibid.*, 126, 1931, 127.

CHAPTER XXIV

THE ACIDS

An acid is a substance which changes blue litmus paper red, and combines with bases to form salts. The substances answering this definition are both inorganic and organic, and among the inorganic acids, as already mentioned, are found both binary and ternary compounds. The four binary acids are hydrochloric acid, HCl, hydrobromic acid, HBr, hydriodic acid, HI, and hydrofluoric acid, HF. These four are called *haloid acids*, because derived from the four halogen elements. Organic acids consist of carbon radicals combined with the group *carboxyl*, $COOH$. These will be discussed under their proper grouping in Part IV.

The inorganic acids are, with the exception of the haloid acids just mentioned, hydroxides of the negative elements. Acids may be solids, liquids, or gases; in fact, all the members of this large group have little in common save their acid action on litmus paper, their ability to form salts with the alkalis and their property of liberating hydrogen ions (see p. 407) when dissolved in water.

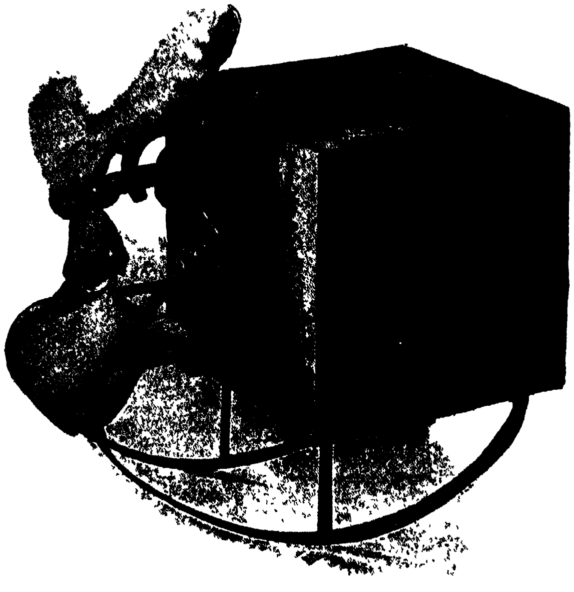


Fig. 258.—Carboy trunnion.

In this chapter we will discuss all the official inorganic acids except boric acid, chromic acid, and arsenous acid, the three being considered under the elements from which derived. All those considered in this chapter are liquids, and several are commercially called the *heavy acids*, because their specific gravity is greater than water. These acids are usually in the concentrated form, and are decidedly caustic. Hence in handling them great care must be taken to avoid bringing them in contact with delicate substances. If, in handling, they are spattered on the skin, they should be immediately washed off; if the area of burn is considerable, it should be covered with emollients of mildly alkaline character, such as lime liniment or sodium bicarbonate. Their active character prevents their ordinary storage in wood or metal, although it might be of interest to mention that sulfuric acid in concentrated form can be safely stored in iron tanks, the metal being attacked only when the acid is in a diluted form. In pharmacy, however, such acids must be handled entirely in glass or porcelain, and in purchasing quantities of the same they are usually furnished in large glass containers boxed with straw, called *carboys*. In handling these carboys it is usually advisable to have trunnions on which they can be rocked (Fig. 258), or else an *acid pump* (Fig. 260) may be employed.

At present, hard rubber is being used for acid carboys and for piping used in transporting acids (Fig. 259); while sulfuric acid is being transported in iron tank cars and concentrated hydrochloric acid is being shipped in wooden tank cars lined with unvulcanized rubber.

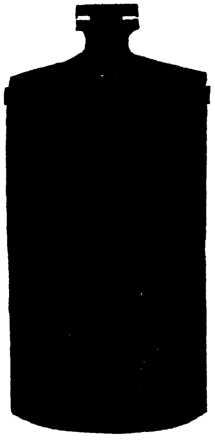


Fig. 259.—American Hard Rubber Company, hard rubber acid carboy.

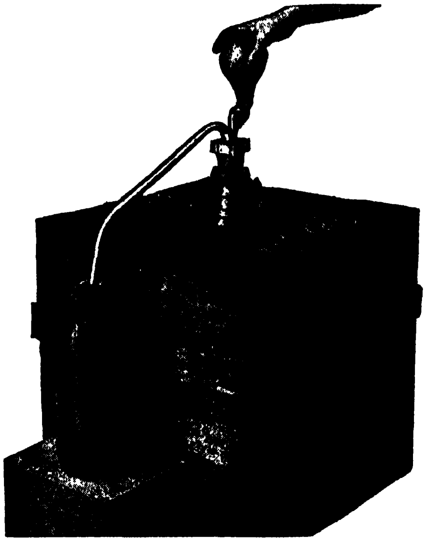


Fig. 260.—Thompson's pneumatic acid pump (Courtesy of Scientific Glass Apparatus Co.).

There is no uniformity in the commercial strength of the different strong acids, the usual custom being to furnish an acid of the greatest concentration feasible.

It is useful to memorize the following strengths and specific gravities:

	HCl	H_2SO_4	HNO_3
Percentage of absolute acid...........	35 to 37	94 to 98	67 to 70
Specific gravity (approximate)	1.175	1.84	1.403

While the pharmacopœial concentrated acids vary in strength, the same standard demands that diluted acids contain 10 per cent of absolute acid, except diluted acetic acid (6 per cent). A convenient method of determining the strength of acids is by their specific gravity. As an illustration, it will be noted above that the specific gravity of sulfuric acid is 1.83. Water, which is the only likely adulterant, has, of course, the specific gravity of 1.00, and if sulfuric acid is diluted with water, the specific gravity will fall to a point somewhere between 1.83 and 1.00. The only official liquid acid whose specific gravity is not a criterion of strength is acetic acid. (See p. 670.) The antidote for acids is mild alkali, such as calcined magnesia or lime liniment, this being a good illustration of a chemical antidote; the mild alkali acting on an acid to form a neutral and inert salt. Too much emphasis cannot be placed on the word "mild," for while it is true that concentrated sodium hydroxide or other strong alkali would form with the acid a neutral salt, yet the action of the same alkali is as dangerously caustic as is the acid for which it is intended as an antidote.

Most inorganic acids are prepared by the action of sulfuric acid on a salt of the acid which is desired. Sulfuric acid possesses a greater affinity for metals than most other acids, hence when a salt of the acid is treated with sulfuric acid, a sulfate is formed and the acid is liberated.

Reviewing the manufacture of official acids, we see how often this rule applies:

Hydrochloric acid, made from sodium chloride and sulfuric acid.
Hydrobromic " " " potassium bromide and sulfuric acid.
Nitric " " " sodium nitrate and sulfuric acid.
Chromic " " " potassium dichromate and sulfuric acid.
Carbonic " " " sodium bicarbonate and sulfuric acid.

Exceptions to this method are:

Phosphoric acid, made by oxidation of phosphorus with nitric acid.
Sulfurous " " reduction of sulfuric acid with carbon.

The officials treated in this chapter are:

Hydrochloric acid	containing	35 to 37	per cent. of	absolute	HCl.
Diluted hydrochloric acid	"	about 10	"	"	HCl.
Diluted hydriodic acid	"	about 10	"	"	HI.
Syrup of hydriodic acid	"	about 1	"	"	HI.
Nitric acid	"	67 to 70	"	"	HNO_3.
Sulfuric acid	"	94 to 98	"	"	H_2SO_4.
Diluted sulfuric acid	"	about 10	"	"	H_2SO_4.
Aromatic sulfuric acid	"	about 20	"	"	H_2SO_4.
Phosphoric acid	"	85 to 88	"	"	H_3PO_4.
Diluted phosphoric acid	"	about 10	"	"	H_3PO_4.
Hypophosphorous acid	"	30 to 32	"	"	HPH_2O_2.

OFFICIAL ACIDS

ACIDUM HYDROCHLORICUM—Hydrochloric Acid

(Acid. Hydrochlor.)

HCl. Molecular weight, 36.47

Hydrochloric Acid is an aqueous solution containing not less than 35 per cent and not more than 37 per cent of HCl.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

Colorless fuming liquid; pungent odor; strongly acid to taste and to litmus; sp. gr. 1.175. For details see U.S.P., p. 20. For *tests for identity*, for *impurities* (bromide, iodide, free chlorine and bromine, heavy metals, arsenic, sulfate, sulfurous acid) and for *assay* see U.S.P., p. 21.

Remarks.—This is an aqueous solution of hydrochloric acid gas, containing 35 to 37 per cent of absolute acid, and having a specific gravity of 1.175. Its two synonyms—*spirit of sea salt* and *muriatic acid*—suggest its origin, the word muriatic being derived from the Latin *muria*, which means brine. It is made by distilling a mixture of salt (sodium chloride) and sulfuric acid; usually as a side-product in the Leblanc process (see p. 483). It can also be made by treating chlorine with steam in the presence of carbon.

ACIDUM HYDROCHLORICUM DILUTUM—Diluted Hydrochloric Acid

(Acid. Hydrochlor. Dil.)

Diluted Hydrochloric Acid is an aqueous solution containing in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of HCl.

Storage.—Preserve in glass-stoppered bottles.

Condensed Recipe.

Mix 236 cc. of hydrochloric acid with enough distilled water to make 1000 cc.

Summarized Description.

Colorless, odorless liquid; strongly acid to taste and to litmus; sp. gr. 1.046. For details see U.S.P., p. 21. For *tests for identity,* for *impurities* (as under hydrochloric acid) and for *assay* see U.S.P., p. 21.

Hydrochloric acid, always in diluted form, is used in indigestion. Loessl finds it of value as an antiseptic when used as a 0.005 per cent solution.

Dose.—Of the diluted acid, 2 cc. (30 minims).

ACIDUM HYDRIODICUM DILUTUM—Diluted Hydriodic Acid

(Acid. Hydriod. Dil.)

HI. Molecular weight, 127.93

Diluted Hydriodic Acid is an aqueous solution containing, in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of HI, and not less than 0.6 Gm. and not more than 1 Gm. of HPH_2O_2.

Caution.—Do not dispense diluted hydriodic acid or employ it in the preparation of other products, if the acid contains free iodine.

Storage.—Preserve in glass-stoppered bottles, in a cool place.

Condensed Recipe.

No recipe given in U.S.P. XI. That of U.S.P. X follows:

Dissolve 135 Gm. potassium iodide in 250 cc. of distilled water. Dissolve 122 Gm. tartaric acid in 400 cc. of diluted alcohol. Mix the two solutions, add 20 cc. of hypophosphorous acid, chill, filter through cotton, wash filter with diluted alcohol. Warm filtrate on water bath until the alcohol has evaporated. Then add enough water to make 1000 Gm.

Summarized Description.

Colorless or faintly yellow liquid; odorless; strongly acid to taste and to litmus; sp. gr. 1.10. For details see U.S.P., p. 19.

For *tests for identity,* for *impurities* (sulfuric acid, barium, free iodine, chlorides, heavy metals, arsenic) and for *assay* see U.S.P., p. 20.

SYRUPUS ACIDI HYDRIODICI—Syrup of Hydriodic Acid

(Syr. Acid. Hydriod.)

Syrup of Hydriodic Acid contains not less than 1.3 Gm. and not more than 1.5 Gm. of HI in each 100 cc.

Condensed Recipe.

Mix 130 cc. of diluted hydriodic acid with 550 cc. of water and dissolve in this 450 Gm. sucrose (sugar) and then add enough water to make 1 liter. For details see U.S.P., p. 372.

Summarized Description.

Colorless or faint straw-colored fluid; odorless; sweet acidulous taste, sp. gr. 1.18. For details see U.S.P., p. 372.

For *tests for identity,* for *impurities* (free iodine) and for *assay* see U.S.P., p. 372.

Remarks.—Hydriodic acid, as mentioned on p. 441, is the binary acid of iodine. It is official in the present Pharmacopœia in the form of diluted (10 per cent) acid and the syrup (containing slightly more than 1 per cent by weight of absolute hydriodic acid). The method of the preparation of the diluted acid, as given in U.S.P. X, is a process devised by Dr. Buchanan, of Glasgow, and antedates the Fothergill-Wade process, which it closely resembles, the acid being liberated from potassium iodide by the addition of tartaric acid sufficient to precipitate potassium bitartrate, the equation being as follows:

$$KI + H_2C_4H_4O_6 = KHC_4H_4O_6 + HI.$$

The recipe of U.S.P. X directed the addition of 1¼ per cent of hypophosphorous acid, U.S.P., which is added to prevent, as far as possible, the separation of the iodine, which occurs when hydriodic acid is exposed to the air, the reaction being as follows:

$$2HI + O \text{ (from air)} = H_2O + I_2.$$

Hypophosphorous acid is supposed to recombine the liberated iodine with hydrogen by the following reaction:

$$HPH_2O_2 + 4I + 2H_2O = 4HI + H_3PO_4.$$

This decomposition, as well as that of ferrous iodide, has been a subject of considerable discussion of late years (see p. 562), recent investigations seeming to show that the accepted idea that the decomposition is due to the separation of free iodine is erroneous. Haussmann claims that spoiled specimens of the syrup contain no free iodine, and that the change noticed is the conversion of the cane sugar into glucose, which change is accompanied by side-reactions, which produce the brown color. His theory, however, as far as syrup of ferrous iodide (p. 562) is concerned, is not in accord with facts, since if the brown tint is due to caramelization of sugar, the syrup could not be restored to its green tint by the introduction of a few card teeth, as really obtains. The author's own research indicates that the presence of hypophosphite as a preservative while advantageous as far as the diluted acid is concerned hinders rather than aids preservation of the syrup and syrup of ferrous iodide. The best way to preserve these syrups is the old-fashioned way of keeping them exposed to sunlight. Since iodine is liberated under oxidizing action of air, it is advisable to avoid combination of the official acid or the syrup prepared therefrom with oxidizing agents; hence potassium chlorate should not be dispensed with the syrup.

The Pharmacopœia of 1880 directed a method for the manufacture of the syrup of hydriodic acid different from that of the present Pharmacopœia, the process of 1880 being to treat water in which iodine was suspended with hydrogen sulfide gas, the equation being as follows:

$$H_2S + I_2 = 2HI + S.$$

As a matter of fact, this process leads to a purer form of hydriodic acid than does the process of U.S.P. X, since the attempt to precipitate all the potassium salt as potassium bitartrate is not entirely successful, inasmuch as the bitartrate is somewhat soluble.

Both the diluted acid and the syrup are used as alteratives.

Dose.—Of diluted acid, 1 cc. (15 minims). Of syrup, 4 cc. (1 fluidrachm).

ACIDUM NITRICUM—Nitric Acid

(Acid. Nitric.)

HNO_3. Molcular weight, 63.02

Nitric Acid contains not less than 67 per cent and not more than 70 per cent of HNO_3.

Storage.—Preserve in glass-stoppered bottles, in a cool place and protected from light.

Summarized Description.

Fuming, caustic, corrosive liquid; suffocating odor; strongly acid to litmus; sp. gr. 1.403; boils at 120° C.; dissolves metals with evolution of red-brown fumes; stains wool and the skin yellow. For details see U.S.P., p. 23.

For ***tests for identity***, for ***impurities*** (nonvolatile matter, arsenic, sulfuric acid, hydrochloric acid, and heavy metals) and for ***assay*** see U.S.P., p. 23.

Remarks.—While nitric acid is ordinarily made by distilling a mixture of Chile saltpetre (sodium nitrate) and sulfuric acid, the enormous demand for the acid during the Great War encouraged its production from atmospheric nitrogen. The general subject, called *nitrogen fixation,* included the Birkeland Eyde process in which nitric acid was directly produced from air; the Haber process in which ammonia is first formed and later oxidized into nitric acid with the use of platinum as catalyst; the Bucher process in which sodium cyanide is first made and later converted into the acid; the cyanamide process and a number of other methods.

In the *Birkeland-Eyde process,* air is passed through tubes containing powerful electric arcs, the apparatus being planned to produce a maximum of N_2O_5 and a minimum of the other oxides of nitrogen. The N_2O_5 is either passed into water (forming nitric acid) or into sodium hydroxide (forming sodium nitrate) or into milk of lime (forming calcium nitrate); the nitrates being easier to ship than the acid itself.

The *Haber process* will be described under ammonia (see p. 502) while the reader is referred to the Bibliography at the end of this chapter for articles describing the other methods.

While official nitric acid is 68 per cent patented processes now permit the production of a 99 per cent acid. In the distillation of nitric acid, acid-resisting iron stills are employed.

The official concentrated acid contains 68 per cent of absolute acid, and has the specific gravity of 1.403. It was formerly largely dispensed under the synonym of *aqua fortis* (strong water), a synonym which, fortunately, is falling into disuse. The danger of the phrase is due to a confusion of it on prescriptions with *aqua fontana,* which means spring water. Nitric acid is one of the most active of chemical substances, it being the most prominent oxidizing agent in general use. (See p. 447.) Great care should be taken in handling it to avoid contact with the skin or clothing, as it acts as a very strong caustic on both, either destroying the fabric or staining it yellow.

Nitric acid is given highly diluted as a tonic and astringent.

Diluted Nitric Acid (U.S.P. VIII) is a 10 per cent preparation made by diluting nitric acid with water according to the rule of dilution by alligation.

SULFURIC ACID

(H_2SO_4)

This well-known substance has been known since the fifteenth century, it being a matter of record that Basil Valentine obtained it by heating ferrous sulfate; from this origin is the synonym, *oil of vitriol,* derived. The alchemists had become familiar with several chemicals of crystalline form and of different colors, such as the sulfates of zinc, copper, and iron. By reason of their similarity to bright pieces of glass these substances were termed respectively *white vitriol* ("vitrous" meaning glass), *blue vitriol,* and *green vitriol.* All three of these "glasses," on being submitted to strong heat in a retort, yielded an oily liquid (sulfuric acid), which was, therefore, called oil of vitriol (or oil of glass).

As already explained the formula, H_2SO_4, is assigned this important acid. Oddo and Anneli state that estimations of its molecular weight points to the double formula $H_4S_2O_8$ and suggest a graphic formula showing this.

Sulfuric acid is the most important manufactured chemical used, being the veritable foundation of modern chemical industry; therefore its process of manufacture must be clearly comprehended.

The first stage is burning sulfur in contact with air, when there is formed sulfurous oxide, SO_2, whose suffocating odor is noticed in burning sulfur.

The second stage is the conversion of sulfurous oxide, SO_2, into sulfuric oxide, SO_3. This occurs by the process of oxidation—the adding of oxygen to a body—a process not so simple as it at first seems. We cannot change SO_2 into SO_3 by simply mixing with oxygen. To accomplish this we have to employ an energetic compound like nitric acid, chromium trioxide, or potassium permanganate. Let us explain the reason for this.

The change from SO_2 to SO_3 is not simply an addition of one more atom of oxygen; there is another and very important difference—that of valence of sulfur.

Sulfur in SO_2 is quadrivalent—has the valence IV—while in SO_3 it is hexivalent—has the valence VI—and to change sulfur with four bonds to sulfur with six bonds requires energetic action. So oxidation is not merely adding oxygen to a body but in inorganic chemistry it almost invariably means change in the valence of one of the elements acted on.

In the sulfuric acid process we have completed the second stage, save giving the equation showing the reaction, which is:

$$3SO_2 + 2HNO_3 = 3SO_3 + N_2O_2 + H_2O.$$

In writing reactions always balance the finished equation to see if the same number of atoms are found on either side of the sign of equality. This is most important, for otherwise the equation is defective. Let us now run over the reasoning whereby the balancing is done. Write down the equations given above, checking off as we go along. 3S, in the SO_2 groups: on the other side of the equation we have 3S in the SO_3 groups, check them. 3×2 O in the SO_2 groups and 2×3 O in the HNO_3 groups; that makes 12 O's in all. Let us look on the other side. 3×3 O in the SO_3 groups; 1 O in the H_2O and 2 O in N_2O_2, they tally; so check them off. Then there are 2H in the HNO_3 groups, and on the other side there are 2H in H_2O; check off. Lastly, here are 2N in the HNO_3 groups, and across the equality lines there are 2N in N_2O_2. When these are checked off, nothing unaccounted for remains on either side.

An interesting and useful point, especially in equation writing, is the amount of oxygen furnished by nitric acid in oxidation. $2HNO_3$ give 3 atoms of oxygen, as is shown in the following equation:

$$2HNO_3 \text{ breaks up into } \begin{cases} H_2\quad O \\ \ \ N_2O_2 \\ \qquad O_3 \end{cases}$$

$$\overline{H_2N_2O_6} = 2HNO_3.$$

The third stage of the sulfuric acid reaction is very simple. The sulfuric oxide, SO_3, comes in contact with steam, H_2O, forming sulfuric acid, H_2SO_4.

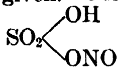
In the second stage one of the products is N_2O_2. This readily takes oxygen from the air, even in the lead chamber, changing from a colorless vapor to the red-brown fumes, N_2O_4 or $2NO_2$. This N_2O_4 is brought in contact with fresh quantities of sulfurous oxide, which it oxidizes into sulfuric oxide by the following reaction: $2SO_2 + N_2O_4 = N_2O_2 + 2SO_3$.

The resulting N_2O_2 is again converted into N_2O_4, and thus the process is continuous, and a small quantity of nitric acid can be used over and over again in the oxidization process. Let us sum up the reaction in its five stages.

I. $S + O_2 = SO_2.$
II. $3SO_2 + 2HNO_3 = 3SO_3 + H_2O + N_2O_2.$
III. $SO_3 + H_2O = H_2SO_4.$
IV. N_2O_2 (from II.) $+ O_2 = N_2O_4.$
V. $2SO_2 + N_2O_4 = 2SO_3 + N_2O_2$
VI. $SO_3 + H_2O = H_2SO_4.$

From this stage on the reaction is continuous, employing I, IV, V, and VI.

There are several intermediate stages in the reaction not shown in the equations just given. For instance, SO_2 and N_2O_4 unite temporarily to form nitrosyl sulfuric acid,



$SO_2(OH)(ONO)$

The appended sketch (Fig. 261) outlines the apparatus in which the reactions occur. The walls of the chamber are lined with lead; not because the metal is impervious to the acid, but because the lead sulfate formed is insoluble in water and sticks to the metal as a protective covering. Were zinc, copper, or iron employed, the sulfates of the metal, being soluble in water, would be dissolved off by the steam, constantly leaving a fresh metallic surface to be attacked.

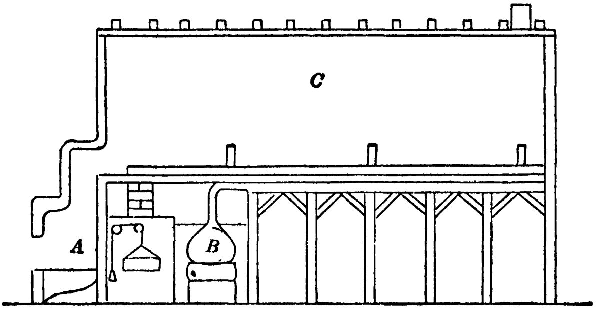


Fig 261.—Lead chamber (schematic): *A*, Sulfur furnace where reaction I takes place; *B*, retort where nitric acid is generated; *C*, lead chamber where reactions II–III occur.

While a deviation from the subject directly under consideration, this is perhaps the best place to emphasize the necessity of learning to write and balance equations correctly—those short-hand representatives of chemical reactions found on almost every page from where first introduced (p. 401). As an illustration of how *not* to write equations may be cited the following remarkable reaction, submitted years ago, the writer by one of his pupils:

$$Zn + NaOH = H_2ZnSO_4!$$

How can a *sulfate* be formed when zinc and sodium hydrate are mixed? When we write, as we should—

$$Zn + 2NaOH = H_2 + Na_2ZnO_2,$$

we mean that if we combine 1 atom of zinc with 2 atoms sodium, 2 atoms oxygen, and 2 atoms hydrogen, we get, as the reaction products, 2 atoms hydrogen and also 2 atoms sodium, 1 atom zinc, and 2 atoms oxygen, and both sides of the equation must, of course, foot up the same.

To use a common comparison: if we take 4 apples, ½ pound sugar, and 1 pound flour to make a pie, the finished pie will surely not contain 8 apples, 1 pound sugar and 10 pounds of flour. Neither will it contain 4 apples and a pound of baking soda. Use, in writing equations, the same common sense employed in discussing an ordinary apple pie, remembering that a chemical reaction is merely a rearrangement of matter, and during such a change matter is neither created nor lost. While on the subject it may be well to emphasize three varieties of reactions by giving equations expressing their character:

A *simple reaction* is one in which two elements combine to form a compound, thus: $H_2 + O = H_2O$.

A *simple decomposition* is a reaction in which an element acts on a compound in such manner as to break it up and then form a new compound, thus: $K + H_2O = KOH + H$.

A *double decomposition* is a reaction in which two compounds so act on each other as to form two new compounds, thus: $KOH + HCl = H_2O + KCl$.

To return to sulfuric acid, besides obtaining sulfurous oxide by burning sulfur in air, the same gas is obtained by the burning of iron pyrites (see p. 552), and in technic this substance is largely used for the production of sulfuric acid in place of sulfur. The objection to this so-called "pyrites acid" is the native pyrites usually contain arsenic, and the acid obtained therefrom is frequently contaminated with this deleterious substance. Careful manufacturers, however, succeed in removing all traces of arsenic by treatment of the crude acid with hydrogen sulfide, the excess of which is removed from the acid by heating. According as to whether sulfur or iron pyrites is employed in the manufacture of the sulfuric acid, specially constructed furnaces are employed. Upon roasting metallic sulfide ores in the processes of metallurgy (p. 533) large quantities of sulfurous oxide are produced. This is now collected from the smelter flues and is converted into sulfuric acid. It might here be said that the limitations of this work preclude entering into details of technic of the manufacture of all the chemicals here described; the student desiring such is referred to standard works on chemical technology found in the preface.

Of recent years, the *contact method* of manufacture of sulfuric acid has come into use. In this process the oxidation of sulfurous oxide to sulfuric oxide is accomplished by passing a mixture of the first-named oxide and of air over spongy platinum heated to 400° to 450° C., thus avoiding the use of nitric acid—the air furnishing the required oxygen and the platinum acting as catalyst (see p. 407). The resulting SO_3 is dissolved in commercial sulfuric acid instead of in water as the latter solvent would react too violently with the sulfuric oxide. The product of the contact process, technically called *oleum*, is a highly concentrated acid running from 100 per cent to 110 per cent H_2SO_4. The latter figure may sound confusing until it is stated that 110 per cent oleum is really $H_2SO_4 + SO_3$ or $H_2S_2O_7$.

Applying molecular proportions we find that $H_2S_2O_7$ has the same amount of sulfuric oxide as $2H_2SO_4$; that

$$\begin{array}{lcc} & H_2S_2O_7 \longrightarrow & H_2SO_4 \\ \text{(Mol. wts.)} & 178 & 2 \times 98 \text{ or } 196 \end{array}$$

If 178 parts of $H_2S_2O_7$ represent 196 parts of H_2SO_4 then 100 parts of $H_2S_2O_7$ represent

$$\frac{100}{178} \times 196 = 110$$

110 parts of H_2SO_4. Hence $H_2S_2O_7$ is really 110 per cent H_2SO_4.

Sulfuric acid is the most important manufactured chemical known to the world, it being used in numberless branches of trade. An indication of its enormous consumption is the statement that in this country in 1929 over 8,000,000 tons of the acid were produced.

Three forms of sulfuric acid are recognized by the Pharmacopœia.

ACIDUM SULFURICUM—Sulfuric Acid

(Acid. Sulfuric.)

H_2SO_4. Molecular weight, 98.08

Sulfuric Acid contains not less than 94 per cent and not more than 98 per cent of H_2SO_4.

Caution.—When mixing sulfuric acid with other liquids the acid should always be added to the diluent, and great caution should be observed.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

Colorless, odorless, oily liquid; very caustic and corrosive; sp. gr., 1.84, miscible with water and with alcohol, with evolution of much heat; vaporizes with evolution of dense fumes. For details see U.S.P., p. 27.

For *tests for identity*, for *impurities* (lead, nitric or nitrous acids, hydrochloric acid, heavy metals, nonvolatile matter, sulfurous acid, arsenic) and for *assay* see U.S.P., p. 27.

Remarks.—This contains 94 to 98 per cent of the absolute acid, and has the specific gravity 1.84. It is a colorless liquid, of oily consistence, miscible in all proportions of alcohol and water with the evolution of so much heat that mixing requires great caution.

ACIDUM SULFURICUM DILUTUM—Diluted Sulfuric Acid

(Acid. Sulfuric. Dil.)

Diluted Sulfuric Acid is an aqueous solution containing, in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of H_2SO_4.

Storage.—Preserve in glass-stoppered bottles.

Condensed Recipe.

Pour 57 cc. sulfuric acid cautiously into 900 cc. distilled water. When cool add enough distilled water to make 1000 cc. For details see U.S.P.

Summarized Description.

Colorless, odorless liquid; strongly acid to taste and to litmus; sp. gr. 1.067. For details see U.S.P., p. 29.

For *tests for identity*, for *impurities* (as given under sulfuric acid) and for *assay* see U.S.P., p. 29.

Remarks.—This diluted form contains about 10 per cent absolute H_2SO_4. As mentioned above, the dilution of the strong acid with either alcohol or water must be performed with care, as great heat is evolved, frequently resulting in a spattering of the hot acid. A rule always to be observed in diluting sulfuric acid is that the acid should be poured in a fine stream into the water contained in a shallow dish. Never should water be poured into the acid, and rarely is it advisable to perform the dilution of the acid in anything but a shallow open dish.

Medical Properties.—Used like aromatic sulfuric acid. The concentrated is never used medicinally except after dilution.

Dose.—1 cc. (15 minims).

ACIDUM SULFURICUM AROMATICUM—Aromatic Sulfuric Acid

(Acid. Sulfuric. Arom.)

Aromatic Sulfuric Acid contains, in each 100 cc., free sulfuric acid and ethylsulfuric acid together equivalent to not less than 19 Gm. and not more than 21 Gm. of H_2SO_4.

Storage.—Preserve in glass-stoppered bottles.

Condensed Recipe.

See below.

Summarized Description.

Clear, reddish-brown liquid; aromatic odor; sp. gr. 0.95. For details see U.S.P., p. 28.

For *tests for identity*, and for *assay* see U.S.P., p. 28.

Remarks.—This pharmaceutic is made by adding 114 cc. of the concentrated acid to 700 cc. alcohol, and when the mixture is cooled, there are added 10 cc. of fluidextract of ginger, 1 cc. of oil of cinnamon, and enough alcohol to make the finished product measure 1000 cc.

At the first glance the above recipe would indicate a 10 or 11 per cent acid, but when it is recalled that the 100 cc. of sulfuric acid will weigh 184 Gm., while 100 cc. alcohol weighs but 82 Gm., it will be seen that the strength by weight is about 20 per cent. This preparation is known as *elixir of vitriol,* and replaces the original recipe, which was popular for several hundred years. The preparation contains, besides sulfuric acid, some ethylsulfuric acid. (See p. 661.)

Aromatic sulfuric acid affords the favorite means of administration of the acid, its chief use being in the night-sweats of tuberculosis.

Dose.—0.5 cc. (8 minims).

Nordhausen sulfuric acid is a form of acid obtained by distilling completely exsiccated ferrous sulfate or roasted iron pyrites in dry retorts. It consists of a mixture of H_2SO_4 and SO_3, and is, therefore, sometimes assigned the formula $H_2S_2O_7$. A semisolid modification now in commerce consists almost entirely of SO_3. As stated on page 449, *oleum* of commerce is a variety of this acid.

ACIDUM PHOSPHORICUM—Phosphoric Acid
(Acid. Phosph.)

H_3PO_4. Molecular weight, 98.04

Phosphoric Acid contains not less than 85 per cent and not more than 88 per cent of H_3PO_4.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

Colorless, odorless, syrupy liquid; strongly acid to taste and to litmus; sp. gr. 1.71; on heating it is converted in pyrophosphoric acid and then into metaphosphoric acid. For details see U.S.P., p. 24.

For *tests for identity* for *impurities* (phosphorous and hypophosphorous acids, heavy metals, arsenic, sulfate, nitrate, phosphate) and for *assay,* see U.S.P., p. 25.

Remarks.—Phosphoric acid is recognized by the Pharmacopœia in the form of an 85 to 88 per cent solution, the so-called "syrupy phosphoric acid." It is made by the oxidation of phosphorus with nitric acid, a process accompanied by some danger, hence the recipe is omitted in the present Pharmacopœia, since the chemical can be best and most cheaply prepared by the large manufacturer. The equation of the reaction is

$$\begin{array}{lllllllll} 6P & + & 10HNO_3 & = & 3P_2O_5 & + & 5H_2O & + & 5N_2O_2 \\ P_2O_5 & + & 3H_2O & = & H_6P_2O_8 & = & 2H_2PO_4. & & \end{array}$$

Let us go over the reasoning employed in figuring out these quantities. We want to make P_2O_5; we need for this 5 atoms of oxygen. We have learned that $2HNO_3$ yield 3 atoms of oxygen; three is not divisible into five; hence to make P_2O_5 will require the amount of oxygen from nitric acid corresponding to the least common multiple of three and five. This is fifteen. Fifteen atoms of oxygen are needed; $2HNO_3$ yield 3 atoms oxygen; hence to furnish 15 O will require 5 × $2HNO_3$ or $10HNO_3$.

We are making P_2O_5. One molecule of this contains 5 atoms of oxygen. We have 15 atoms of oxygen; hence we can make $3P_2O_5$; for $3 \times 5 O = 15 O$. Lastly, we see that in $3P_2O_5$ there are six phosphorus; hence we begin the equation with 6 atoms of phosphorus and 10 molecules of nitric acid.

If to one molecule of P_2O_5 we add 1 molecule of H_2O, we get 2 molecules of metaphosphoric acid, HPO_3. If, on the other hand, as above, we add 3 molecules H_2O to 1 molecule of P_2O_5, we get 2 molecules of the official (so-called "ortho-") phosphoric acid, H_3PO_4.

A less dangerous method of manufacture than that just given, devised by Professor Markoe for the use of the retail pharmacist, consisted in treating phosphorus under the surface of water with bromine and a small quantity of iodine, and at the end of the reaction nitric acid is added. The reaction runs in three distinct stages. First, phosphorus and bromine unite to form phosphorus pentabromide, viz.:

$$\text{(I) } P + Br_5 = PBr_5.$$

This decomposes in the presence of water, with the formation of phosphoric acid and hydrobromic acid:

$$\text{(II)} \quad PBr_5 + 4H_2O = H_3PO_4 + 5HBr.$$

The nitric acid liberates bromine from hydrobromic acid:

$$\text{(III)} \quad 6HBr + 2HNO_3 = 3Br_2 + 4H_2O + N_2O_2.$$

The bromine here freed acts on another portion of the phosphorus, and the reactions I, II, and III are repeated in regular order as long as any phosphorus remains unoxidized.

It will be seen that the ultimate results of this process is the same as that of the first process, nitric acid being the real oxidizing agent in both cases. The function of the bromine in the second process is to lessen the violence of the reaction by gently bringing the nitric acid in contact with the phosphorus, insuring a gradual evolution of the gaseous nitrogen dioxide; for be it remembered that most explosions are due either to a sudden evolution or a sudden contraction of a gas. If the process is so planned as to permit the evolution of a gas during several hours, no danger ensues, but if the same amount of gas is evolved in a few moments, a violent explosion occurs (p. 471).

In both processes the liquid remaining upon completion of reaction is evaporated, partly to remove the last traces of nitric and nitrous acids (also bromine, in last process), and also to concentrate the product to the official strength. The last task which is done by the manufacturer either in a vacuum apparatus or by spraying upon a rapidly revolving heated disk (see p. 874), is very tedious if carried out in an open evaporating dish, and in the writer's experience he has never succeeded in making an acid of pharmacopœial strength, the strongest he produced being about 65 per cent. Under the Pharmacopœia of 1880, where a 50 per cent acid was directed, the Markoe process was feasible for the retail pharmacist, but now that the Pharmacopœia demands the more concentrated form, we are brought back to the original proposition that the pharmacist should purchase his phosphoric acid.

There has lately been developed a process of manufacture of P_2O_5 by roasting phosphate rock with coke in the presence of an abundance of air; the resulting P_2O_5 being condensed in a tower by the electric precipitation method.

Much of the phosphoric acid of commerce contains arsenic, and the origin of this impurity is of interest as showing how persistently impurities may sometimes cling to chemicals, even though the original substance has undergone several changes. The arsenic in the phosphoric acid is due to arsenic-contaminated phosphorus. The phosphorus obtains it from arsenic-contaminated sulfuric acid, while the sulfuric acid contaminated with arsenic is usually that manufactured from iron pyrites, in which the arsenic originally occurred. It, therefore, behooves every careful pharmacist to test both his phosphoric acid and his sodium phosphate for arsenic by the tests prescribed in the Pharmacopœia. (See Part V.)

ACIDUM PHOSPHORICUM DILUTUM—Diluted Phosphoric Acid

(Acid. Phosph. Dil.)

Diluted Phosphoric Acid is an aqueous solution containing, in each 100 cc., not less than 9.5 Gm. and not more than 10.5 Gm. of H_3PO_4.

Storage.—Preserve in glass-stoppered bottles.

Condensed Recipe.

Mix 69 cc. phosphoric acid with enough distilled water to make 1000 cc.

Summarized Description.

Clear, colorless, odorless liquid; strongly acid to taste and to litmus; sp. gr. 1.057. For details see U.S.P., p. 25.

For *tests for identity*, for *impurities* (as given under phosphoric acid) and for *assay* see U.S.P., p. 25.

Remarks.—This body represents the strong acid diluted with a sufficient quantity of water to make it contain 10 per cent of absolute H_3PO_4. These two acids are employed as nervous stimulants, although for such purpose that popular remedy, *acid phosphates,* is more frequently employed. A recipe for this preparation may be found in the N.F. V under the title of *liquor phosphatum acidus.*

It will be observed that the theoretic construction of the phosphoric acid is based on the addition of 3 molecules of water to 1 molecule of phosphoric oxide, this yielding H_3PO_4—the so-called "orthophosphoric acid." As explained on p. 396 this substance is not the true "ortho-" acid. If the same oxide is combined with 1 molecule of water, the following reaction occurs:

$$P_2O_5 + H_2O = 2HPO_3,$$

metaphosphoric acid being formed. This metaphosphoric acid is called *glacial phosphoric acid,* because on cooling it becomes a transparent, ice-like solid.

Under this division mention may be made of *pyrophosphoric acid,* $H_4P_2O_7$. The composition of this body will be considered when discussing sodium pyrophosphate (p. 496), and mention is here made merely to call attention to the test distinguishing between the three forms, *ortho-*, *meta-*, and *pyro*-phosphoric acids, these three being also called respectively the tribasic, monobasic, and the tetrabasic phosphoric acids. (See p. 396.) Orthophosphoric acid does not coagulate albumin (white of egg), and forms a yellow precipitate of silver phosphate on the addition of silver nitrate solution. Metaphosphoric acid coagulates albumin, and gives a white precipitate with silver nitrate, while pyrophosphoric acid does not coagulate albumin, and gives a white precipitate with silver nitrate. Silver nitrate reactions also apply to the salts of these acids, but the albumin test can be used only with the free acids.

Dose.—1 cc. (15 minims).

Liquor Phosphatum Acidus (N.F. V) or *solution of acid phosphates* is now made by dissolving precipitated chalk and magnesium carbonate in a diluted phosphoric acid, the former method of preparation from bone ash (p. 432) being abandoned.

ACIDUM HYPOPHOSPHOROSUM—Hypophosphorous Acid (Acid. Hypophosph.)

HPH_2O_2. Molecular weight, 66.04

Hypophosphorous Acid is an aqueous solution containing not less than 30 per cent and not more than 32 per cent of HPH_2O_2.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

Colorless or faint-yellow, odorless liquid; strongly acid to taste and to litmus; sp. gr. 1.13; on heating it decomposes into phosphine and phosphorous acid. For details see U.S.P., p. 22.

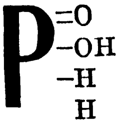
For *tests for identity*, for *impurities* (barium, oxalate, heavy metals, arsenic) and for *assay* see U.S.P., p. 22.

Remarks.—This official contains 30 to 32 per cent of absolute hypophosphorus acid. The usual method of manufacture is by a modification of the Fothergill process, potassium hypophosphite being treated with enough tartaric acid to precipitate all the potassium in the form of insoluble potassium bitartrate. Among other processes which have been suggested is the treatment of calcium hypophosphite with oxalic acid or ammonium oxalate in which case the following reaction occurs:

$$Ca(PH_2O_2)_2 + H_2C_2O_4 = 2HPH_2O_2 + CaC_2O_4.$$

the calcium oxalate being then filtered from the solution of the acid. A third process is by treatment of barium hypophosphite with sulfuric acid, precipitated barium sulfate being removed by filtration.

The Pharmacopœia writes the formula of hypophosphorous acid HPH_2O_2. This is because it has but one replaceable hydrogen. Its composition has been the subject of considerable discussion, but now its graphic formula is supposed to be



$$P\begin{cases}=O\\-OH\\-H\\\ \ H\end{cases}$$

The valence of phosphorus is five, just as in phosphoric acid. This is totally different from what we usually find in various acids of the same element, and constitutes one of the weak points in the valence theory.

Dose.—0.2 cc. (3 minims).

Diluted Hypophosphorous Acid (U.S.P. IX) is a 10 per cent preparation made by diluting the official acid with water. Dose, 0.5 cc. (8 minims).

Acidum Hydrobromicum Dilutum (U.S.P. IX) is a liquid containing 10 per cent of absolute hydrogen bromide, HBr, and since an unstable chemical, should be dispensed as fresh as possible by the pharmacist. Hence efforts have been made to devise a simple method for its extemporaneous manufacture. The ordinary method of manufacture is by treatment of potassium bromide with sulfuric acid by the following reaction:

$$2KBr + H_2SO_4 = 2HBr + K_2SO_4.$$

From this equation it will be seen that the product of the reaction other than hydrobromic acid is potassium sulfate. This dissolves in water with the hydrobromic acid, and to separate the acid from the sulfate solution the tedious process of distillation is necessary. This led investigators to attempt the separation of the second reaction product from the acid by precipitation, in which case the acid could be obtained by simple filtration of the liquid from the precipitate. There are very few insoluble potassium salts, the best known being the bitartrate—cream of tartar—and this is utilized in the Fothergill process of making hydrobromic acid. In this, instead of using sulfuric acid with potassium bromide, tartaric acid is employed, and, on standing, the bitartrate crystallizes out, the reaction being:

$$\underset{119}{KBr} + \underset{150}{H_2C_4H_4O_6} = \underset{188}{KHC_4H_4O_6} + \underset{80}{HBr}$$

The above equation implies the molecular proportion of 119 Gm. potassium bromide and 150 Gm. tartaric acid in making 80 Gm. hydrobromic acid. Then to make 1000 Gm. 10 per cent hydrobromic acid (containing 100 Gm. absolute acid) will require $\frac{100}{80} \times 119$, or 148 Gm. potassium bromide and $\frac{100}{80} \times 150$, or 187 Gm. tartaric acid.

These proportions do not agree with the original recipe of Dr. Wade, who planned an acid each drachm of which would contain the equivalent of 10 grains of bromine; nor with Dr. Fothergill's recipe, which was a cumbersome one, adapted to the Imperial system of measures; nor with the simpler recipe of Professor Maisch.

The latter recipe consists of 80 grains of potassium bromide dissolved in 6 fluidrachms water; 100 grains tartaric acid dissolved in 2 fluidrachms water; the solutions mixed and then chilled, in order to facilitate the separation of the cream of tartar. The difficulty in striking an exact recipe is due to the uncertainty of the amount of cream of tartar precipitated. It must be said that the product of this process is not absolutely pure acid; it always contains some potassium bromide and potassium bitartrate.

Diluted hydrobromic acid is used as a sedative.

Dose.—1 cc. (15 minims).

Acidum Nitrohydrochloricum (N.F. VI) is made by cautiously mixing 18 cc. of nitric acid with 82 cc. of hydrochloric acid.

Acidum Nitrohydrochloricum Dilutum (N.F. VI) is made by diluting 22 cc. of nitrohydrochloric acid with enough distilled water to make 100 cc.

Strong nitrohydrochloric acid is the *aqua regia* of the alchemists. Hydrochloric acid will not dissolve gold, neither will nitric acid; but the two combined have this power, hence the alchemistic name, which, translated, means the king of waters (*royal water*), since it dissolves gold, the king of metals. This special solvent power is due to presence, in the acid, of nitrosyl chloride, NOCl, and free chlorine.

Aqua regia is made by the direct combination of nitric and hydrochloric acids, the reaction being as follows:

$$HNO_3 + 3HCl = NOCl + Cl_2 + H_2O.$$

On figuring at the combining quantities used in the above equation and expressing same in terms of the official strength of the acid, it will be seen that the combining proportion is as follows:

Molecular Weight of Nitric Acid	*Molecular Weight of Hydrochloric Acid*	*Molecular Weight of Nitrosyl Chloride*	*Molecular Weight of Water*
H = 1	H = 1	N = 14	H_2O = 18
N = 14	Cl = 35.5	O = 16	*Molecular Weight of Chlorine*
O_3 = 48	HCl Mol. wt. = 36.5	Cl = 35.5	
HNO_3 Mol. wt. = 63	3HCl = 109.5	NOCl = 65.5	Cl_2 = 71

Repeating the equation:

$$\begin{array}{ccccccccc} HNO_3 & + & 3HCl & = & NOCl & + & Cl_2 & + & H_2O \\ 63 & & 109.5 & & 65.5 & & 71 & & 18, \end{array}$$

we see that the proportions expressed are 63 Gm. absolute (100 per cent) HNO_3 and 109.5 Gm. absolute (100 per cent) HCl. Then, how much 68 per cent HNO_3 and how much 36 per cent HCl will be needed? Taking up the nitric acid problem first, we find it will require $\frac{100}{68} \times 63$ Gm., which equals 92.6 Gm. nitric acid U.S.P. (68 per cent).

As to the hydrochloric acid, we will need:

$\frac{100}{36} \times 109.5$ Gm., which equals 304.1 Gm. hydrochloric acid U.S.P. (36 per cent). That is, 92.6 Gm. official nitric acid, sp. gr. 1.403 and 304.1 Gm. of hydrochloric acid, sp. gr. 1.175, are required to fulfil molecular proportions. Then, how many cubic centimeters of each acid?

As to nitric acid:

1 cc. water = 1 Gm.
1 cc. nitric acid = 1.403 Gm.

Hence, 92.6 Gm. nitric acid equals 92.6 divided by 1.403, which equals 66 cc. As to hydrochloric acid:

1 cc. water = 1 Gm.
1 cc. hydrochloric acid = 1.175 Gm.

Hence, 304.1 Gm. hydrochloric acid equals 304.1 divided by 1.175 equals 258.8 cubic centimeters. That is, nitrohydrochloric acid can be made by mixing 66 cc. nitric acid U.S.P. with 258.8 cc. hydrochloric acid U.S.P., or by union of 18 cc. nitric acid with 71 cc. hydrochloric acid:

$$66 : 258.8 :: 18 : x. \qquad x = \frac{258.8 \times 18}{66} = 71.$$

Comparison of these figures with the N.F. recipe shows the latter provides an excess of hydrochloric acid. The N.F. VI formula is based upon U.S.P. x HCl which was a 32 per cent acid with sp. gr. 1.155.

Diluted nitrohydrochloric acid is made by mixing 22 cc. of nitrohydrochloric acid with enough distilled water to make 100 cc. This contains the equivalent of 3.8 per cent absolute nitric acid and 6.7 per cent absolute hydrochloric acid—that is, about 10 per cent mixed acids. At first glance it would be seen that the same results could be obtained by blending together the same proportion of diluted nitric acid and diluted hydrochloric acid as is directed of the two concentrated acids, and this without the necessity of adding extra water. But in practice the preparation must never be made by combining the acids in diluted form, as then they would have a simple mixture of the two acids and not a solution of nitrosyl chloride and chlorine.

This recalls the fact that chemical reaction usually occurs best in fairly concentrated solution; that the more diluted the solution, the slower and less violent the reaction, for violence of reaction means simply the accomplishment of a large amount of work in a short space of time. Accordingly, if it is known that a reaction is apt to be very violent, its dangers may be lessened by a proper dilution of the ingredients. Another valuable controller of violent reactions is judicious cooling of the vessel.

In mixing the strong acid, care must be exercised, else an effervescence of explosive violence will occur. The Formulary directs that the mixing be done "in a loosely stoppered container" but a large evaporating dish is safer. Note that the Formulary directs that the acid be stored in half-filled amber-colored bottles and states that the acid should not be dispensed if it fails to liberate iodine from potassium iodide solution.

Nitrohydrochloric acid is a hepatic stimulant when given in largely diluted doses. A prescription for liver troubles, formerly largely used, consisted of a mixture of fluidextract of taraxacum with the acid. When these two liquids are mixed, a violent effervescence occurs, due to the oxidation of some of the constituents of the fluidextract. In dispensing such preparations, therefore, care must be taken to avoid bottling until the effervescence ceases, as otherwise the liberated gases will cause an explosion of the bottle and the spattering of the acid mixture.

Dose.—Of strong acid, 0.2 cc. (3 minims). Of official diluted acid, 1 cc. (15 minims).

Persulfuric Acid, $H_2S_2O_8$, and persulfates are now used as powerful oxidizing agents. It is assumed that the eighth oxygen atom is tetravalent as already explained under hydrogen dioxide (see p. 417).

Tetrathionic Acid, $H_2S_4O_6$, and tetrathionates are briefly discussed on page 427.

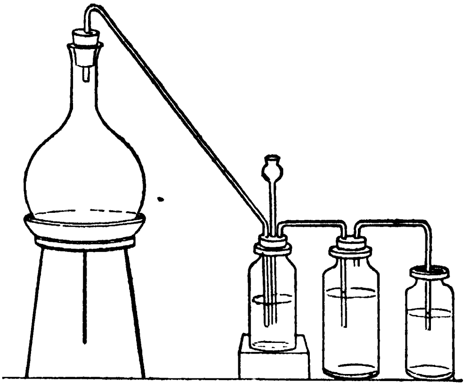


Fig. 262.—Apparatus for manufacture of sulfurous acid.

Acidum Sulfurosum (U.S.P. VIII), or *sulfurous acid,* is a saturated aqueous solution of sulfurous oxide, containing 6 per cent SO_2. In common with all ternary acids, this body is derived from the corresponding oxide, sulfurous oxide, which we have already learned is SO_2, and this combines with water, as shown in the following equation:

$$SO_2 + H_2O = H_2SO_3.$$

While theoretically all ternary acids are derived from the oxides by treatment with water, in the practical manufacture of ternary acids this method is not always evident. For instance, in the Markoe process of manufacture of phosphoric acid (p. 451) the formation of the oxide, while occurring, is not expressed in the equation. Sulfurous acid, however, is manufactured by the direct solution of sulfurous oxide gas in water, this gas being obtained by the reduction of sulfuric acid.

Two operations—oxidation, or the addition of oxygen to a body, and reduction, or the removal of oxygen from a substance—are very important operations in chemical work.

Substances capable of increasing the valence of an element at the same time it gives oxygen to the element are called oxidizing agents, and, on a preceding page, nitric acid, potassium permanganate, and chromic acid were cited as oxidizing agents. A reducing agent, on the other hand, takes oxygen from a body and reduces the valence of one of its elements. Carbon (charcoal), metallic sodium (chiefly as sodium alcoholate), and glucose are examples of reducing agents, and usually in inorganic chemistry carbon is employed. This is true in the manufacture of sulfurous acid, in which the reaction is as follows:

$$\begin{aligned} H_2SO_4 &= SO_3 + H_2O \\ 2SO_3 + C &= 2SO_2 + CO_2. \end{aligned}$$

Both gases formed, sulfurous oxide and carbonic oxide, after washing—after passing through a flask containing water, which will absorb such soluble impurities as sulfuric oxide—are run into cooled distilled water, which dissolves the sulfurous oxide (forming corresponding acid), while most of the carbon dioxide passes off. Since the process affords a striking illustration of the apparatus required in the manufacture, washing, and collecting of gases, a picture of the apparatus is here given (Fig. 262). Sulfur dioxide and sulfurous acid are employed because of their reducing action, both abstracting oxygen from many substances with which they come in contact. It is because of this property that these bodies are used as bleaching agents and as disinfectants, and it is because of the latter action that the official acid is of value in medicine. Sulfurous acid is sometimes used internally as an antiferment. It soon loses the dissolved sulfurous oxide, hence should be dispensed only in the fresh state.

BIBLIOGRAPHY

Hydrochloric Acid.—(History) B. Valentine, Wootton, 1, 1910, 228; Glauber, Wootton, 1, 1910, 263 and 369; Anon., Jl. Soc. Ind., 42, 1923, 386; Holmyard, Jl. Soc. Ch. Ind., 43, 1924, 655. (Manufacture) Hirschkind, *ibid.*, 17, 1925, 1071. (Antiseptic value) Loessl, C.A., 24, 1930, 3861.

Hydrobromic Acid.—(Manufacture) Wade, Dr. Circ., 21, 1877, 108; Fothergill, Dr. Circ., 21, 1877, 83; Maisch, A.J.P., 49, 1877, 42.

Hydriodic Acid.—(Manufacture) Dunn, A.Ph.A., 16, 1868, 383. Husa, Jl. A.Ph.A., 20, 1931, 759; Whitehead, C.A., 25, 1931, 1752. (Darkening) Hausmann, A.J.P., 72, 1900, 217; Horn, A.J.P., 82, 1910, 151. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1154.

Nitric Acid.—(History) Gmelin-Kraut, 1^{1}, 1907, 290; Holmyard, Jl. Soc. Ch. Ind., 43, 1924, 658. (Formula) Brunetti and Ollano, C.A., 26, 1932, 919. (Manufacture) Kuhlmann, Ph. Jl., [2], 4, 1862, 155; Zeisberg, Ch. Met. Eng., 24, 1921, 448. Cuno, Jl. Ind. Eng. Ch., 18, 1926, 1298; Pascal, C.A., 19, 1925, 1327. (Synthesis from ammonia) Malyarevskii, C.A., 22, 1928, 3266; Taylor, Jl. Ind. Eng. Ch., 19, 1927, 1250; Parsons, *ibid.*, 19, 1927, 789; Milbauer, C.A., 23, 1929, 1475; Miravalles, *ibid.*, 22, 1928, 3267; Waeser, *ibid.*, 22, 1928, 4205; Libinson, *ibid.*, 23, 1929, 3307; Kaltenbach, Jl. Soc. Ch. Ind., 48, 1929, 471B; Faüser, *ibid.*, 50, 1931, 535B. (Concentration) U. S. Pat., 1,362,418 and 1,590,043, 1921; Brit. Pat., 150,836, 1919; Can. Pat., 206,819, 1920; Germ. Pats., 305,171, 1916 and 310,081, 1918; Fronchot, Jl. Ind. Eng. Ch., 16, 1924, 235.

Nitrogen Fixation.—(Processes) Eyde, Proc. 8th Int. Cong. App. Ch., 28, 1912, 169; Scott, C.A., 9, 1915, 1273; Summers, Ch. News, 113, 1916, 19; Nauchkoff, Met. Ch. Eng., 17, 1917, 525; Maxted, Ph. Jl., 99, 1917, 62; Bucher, Jl. Ind. Eng. Ch., 9, 1917, 233; Freeman, Ch.-News, 117, 1918, 205 and 231; Brown, Pract. Dr., 36, Aug., 1918, 38; White, Jl. Ind. Eng. Ch., 11, 1919, 231; Pascal, C.A., 14, 1920, 3127; Harker, C.A., 15, 1921, 3543; Haber, Jl. Ind. Eng. Ch., News Ed., 6, May 10, 1928, 9; Slade, Jl. Soc. Ch. Ind., 49, 1930, 760. (Trade statistics) Habsbaum and Grigioni, *ibid.*, 36, 1917, 62; Furness, *ibid.*, 44, 1925, 1241; Crowley, *ibid.*, 45, 1926, 799; Edit, *ibid.*, 48, 1929, 671; Dyes, *ibid.*, 48, 1929, 729; Brand, Jl. Frank. Inst., 207, 1929, 665; Jodidi, *ibid.*, 208, 1929, 767; Howard, Jl. Soc. Ch. Ind., 50, 1931, 265.

Nitrohydrochloric Acid.—(History) Kopp, 3, 1845, 348. (Preparation) Priwozink, C.A., 5, 1911, 41; Goldschmidt, A., 205, 1880, 372. (Composition) Moore, Jl. Am. Ch. Soc., 33, 1911, 1091; Briner, Ch. News, 113, 1916, 215; Lynn and Shoemaker, Jl. A.Ph.A., 15, 1926, 174; Heberlein, Briner and co-workers, C.A., 21, 1927, 3301.

Sulfuric Acid.— (History) Lassar-Cohn, "Things Chemical," January, 1907; Arny, Am. Dr., 39, 1901, 3; Armstrong, Jl. Soc. Ch. Ind., 41, 1922, 257T. (Structure) Berzelius, Thorpe's Dict., 5, 1913, 341; Oddo and Anelli, Ch. Zt., 35, 1911, 837; Brady, Ph. Jl., 126, 1931, 542; Anon., Jl. Soc. Ch. Ind., 50, 1931, 95. (Lead chamber process) Lunge and Berl, Zt. angew. Ch., 19, 1906, 897, 857, and 881; Raschig, Zt. angew. Ch., 23, 1910, 2241; Berl, Zt. angew. Ch., 23, 1910, 2250; Raschig, Jl. Soc. Ch. Ind., 30, 1911, 166; Divers, Jl. Soc. Ch. Ind., 30, 1911, 594; Hempel, C.A., 8, 1914, 3351; Waggaman, C.A., 9, 1915, 3331; Larison, C.A., 11, 1917, 386; Downs, Jl. Soc. Ch. Ind., 46, 1926, 188T.; Berl and Saenger, C.A., 25, 1931, 3440; Mueller, Jl. Soc. Ch. Ind., 44, 1931, 821. (Contact process) Knietsch, B., 34, 1901, 4069; Herreshoff, Jl. Am. Ch. Soc., 30, 1908, 44; Woehler, Foss and Pleuddermann, B., 39, 1906, 3458; ; Lewis and Ries, Jl. Ind. Eng. Ch., 17, 1925, 593 and 19, 1927, 830; Neumann and co-workers, Jl. Soc. Ch. Ind., 47, 1928, 891B; Jaeger, *ibid.*, 48, 1929, 94B.; Holmes and co-workers, Jl. Ind. Eng. Ch., 21, 1929, 850; Spangler, *ibid.*, 21, 1929, 417; Dinsmore, Jl. Soc. Ch. Ind., 50, 1931, 755B; Alhopuro, C.A., 25, 1931, 2247; Fischler, *ibid.*, 26, 1932, 259; Thompson, *ibid.*, 26, 1932, 1069. (Consumption) Wedge, 8th Inter. Cong. App. Ch., 2, 1912, 241; Anon., Ch.

Trade Jl., 57, 1915, 6; Baekeland, Jl. Ind. Eng. Ch., 7, 1915, 978; Anon., Ph. Jl., 98, 1917, 178; Anon., Jl. Soc. Ch. Ind., 43, 1924, 1284; Anon., Ch. Met. Eng., 39, 1932, 42.

Elixir of Vitriol.—(History) Anon., Ph. Jl., [2], 5, 1863, 109. (Manufacture) Anon., A.J.P., 13, 1842, 174. (Properties) Walker, Ph. Jl., 106, 1921, 130. (Assay) Kelly and Krantz, Jl. A.Ph.A., 9, 1920, 775; Smith and Hamilton, Jl. A.Ph.A., 19, 1930, 145.

Persulfuric Acid.— Palme, C.A., 15, 1921, 1469.

Tetrathionates.—Calzolari, C.A., 9, 1915, 2845.

Phosphoric Acid.—(Manufacture) Hüttner, A.Ph.A., 57, 1909, 250; Markoe, A.Ph.A., 23, 1875, 677; La Bour, Ch. Met. Eng., 24, 1921, 466; Waggaman, Jl. Ind. Eng. Ch., 16, 1924, 176; Waggaman, Jl. Ind. Eng. Ch., 16, 1924, 176; Hammond, C.A., 25, 1931, 3131. (Arsenic) in Anon., Dr. Circ., 44, 1900, 151 and 174. (Ortho-, meta- and para-types) Graham, Phil. Trans., 52, 1833, 253; Dobbin, Ch. and Dr., 109, 1928, 643.

Hypophosphorus Acid.—(Structure) Mitchell, Jl. Soc. Ch. Ind., 42, 1923, 181. (Manufacture) Heikel, A.J.P., 80, 1908, 583.° (Use) Anon., Jl. A.M.A., 62, 1914, 1347.

CHAPTER XXV

THE METALS—POTASSIUM

The elements thus far considered are grouped in the class which are called nonmetals or metalloids. As already mentioned, however, a sharp distinction between the positive and the negative elements is a matter of considerable difficulty, and even so it is difficult to decide whether a given element is metallic or nonmetallic. In choosing a definition for the *metals*, about all that can be said is that those substances are metals which possess a metallic luster and which are good conductors of electricity. Their oxides, when they dissolve in water, usually have an alkaline reaction, although several of the elements which we are now to consider will be found to possess oxides which are more acid than basic. It, therefore, reduces the definition to the one statement that metals are good conductors of electricity.

The alkaline metals are the group of elements, lithium, sodium, and potassium, to which is added the radical, ammonium (NH_4), it possessing properties so similar to the three metals just mentioned that its compounds are considered with them. It might be added, too, that the rare elements rubidium and cæsium belong to this group, but since they have no pharmaceutic application, nothing need be said of them in this work.

These alkaline metals possess many characteristics in common. They all possess the valence I, are soft and easily oxidizable substances, and are the only metals whose carbonates are soluble in water. This fact is used in analytic chemistry for separating the salts of these four metals from the other metals, as will be seen in Part V.

POTASSIUM

Symbol, K. Atomic weight, approximately 39

This element is found in *carnallite*, which is a mixture of potassium and magnesium chlorides, and in *sylvite*, which is chiefly potassium chloride—these two ores are obtained from the mines of Stassfurt, Germany and in Alsace, France, Russia, and lately (1931) in New Mexico. Another source of potassium is *suint*, or the washings of wool. The freshly sheared wool is roughly cleaned by washing in water, the washings are then concentrated, and from them is obtained wool fat by extraction with the proper solvent. In the residue is found potassium in sufficiently large amounts to be a commercial source of the element. Potassium carbonate is also extracted from the residues in the manufacture of beet sugar (*vinasse*), while large amounts are obtained from ashes of wood by lixiviation. During the Great War, the German potash was not available to this country and American sources such as seaweed, alkaline lake water, and the flue dust of cement plants were successfully worked. Because of the scarcity of potassium salts during the war, corresponding sodium compounds became more popular.

Potassium was isolated by Sir Humphrey Davy in 1807 in his classic researches in electricity. He submitted potassium hydroxide to electrolysis, placing a small lump on a piece of platinum foil, which was then connected with the negative pole of the battery. Bringing the positive pole in contact with the molten hydroxide the latter dissociated and small globules of metallic potassium were formed.

The electrolysis of potassium in Davy's day was too expensive a process for commercial application, and the metal was first produced commercially by Brunner by another process—by heating potassium carbonate with carbon in a retort to 1000° C., when potassium and carbon monoxide were produced, as shown in the following equation:

$$K_2CO_3 + C_2 = K_2 + 3CO.$$

This process is accompanied by danger, inasmuch as carbon monoxide forms with potassium, as well as with several other metals (copper, for example), well-defined solid carbonyl derivatives. In the isolation of potassium the carbonyl, KCO, clogs up the delivery tube leading from the retort, and with the stoppage of this outlet, explosion of the retort occurs. This danger has been avoided by arranging the apparatus, whereby a plunger is made to fit in the delivery tube, and by passing this plunger up and down the obstructions were removed. It should have been stated that the delivery tube terminates in a vessel containing liquid petroleum or benzin, in order that the potassium will be condensed in a medium by which it is not affected, and which will protect it from atmospheric action.

Potassium is now being made on a large scale by electrolysis of potassium hydroxide, the reduction in the cost of the production of electricity since Davy's day permitting the commercial application of Davy's process.

Potassium is a silvery metal lighter than water (sp. gr. 0.862) and of the consistence of wax, hence it can be readily cut with a knife. A freshly cut surface, after exposure to air, becomes white and granular, due to the formation of the potassium carbonate. Metallic potassium combines so readily with oxygen that when exposed to the air the action is so energetic that the metal is likely to burn. Likewise, when the metallic potassium is thrown on the surface of water it combines with the same, forming potassium hydroxide, as shown in the following equation:

$$K + H_2O = KOH + H,$$

and the heat of the reaction is sufficient to cause an ignition of the hydrogen, which burns with explosive violence. Hence great care should be taken in the handling of potassium, and particular caution must be exercised in combining it with water. For this reason the metallic potassium is always kept under substances devoid of oxygen, such as benzin or petroleum.

The statements just given emphasize the care to be used in handling potassium. In weighing it one rapidly cuts from the piece the oxidized exterior and then presses the pure metal of the interior rapidly between filter paper to remove the last traces of the liquid in which it has been kept. Thus it can be weighed upon a watch glass, although in cases of large quantities it is best to weigh same under petroleum, leaving the drying of the metal until it has been weighed.

The tests for potassium are, first, the characteristic crystalline precipitate that potassium salts yield with platinic chloride. The separation of this precipitate is facilitated by the addition of a few drops of alcohol to the concentrated aqueous solution. Another test is the white, crystalline precipitate of cream of tartar, produced when a potassium salt is brought in contact with the proper quantity of tartaric acid, as shown in the following equation:

$$KCl + H_2C_4H_4O_6 = KHC_4H_4O_6 + HCl.$$

One of the most sensitive tests is the violet tint imparted to a colorless flame.

THE OFFICIAL COMPOUNDS AND PREPARATIONS OF POTASSIUM

Potassium acetate, 99 per cent absolute $KC_2H_3O_2$.
Potassium bicarbonate, 99 per cent absolute $KHCO_3$.
Potassium bitartrate, 99.5 per cent absolute $KHC_4H_4O_6$.
Potassium bromide, 98.5 per cent absolute KBr.
Potassium carbonate, 99 per cent absolute K_2CO_3.
Potassium chlorate, 99 per cent absolute $KClO_3$.
Potassium citrate, 99 per cent absolute $K_3C_6H_5O_7.H_2O$.
Effervescent potassium citrate contains 20 per cent official citrate.
Solution of potassium citrate (N.F. VI) contains 8 Gm. anhydrous citrate per 100 cc.
Potassium and sodium tartrate, 99 per cent absolute $KNaC_4H_4O_6.4H_2O$.
Potassium hydroxide, 85 per cent absolute KOH.
Solution of potassium hydroxide (N.F. VI) contains about 5 Gm. absolute KOH per 100 cc.
Potassium iodide, 99 per cent absolute KI.
Potassium nitrate, 99 per cent absolute KNO_3.
Potassium permanganate, 99 per cent absolute $KMnO_4$.
Sulfurated potassa, 12.8 per cent S.

We might also add—

Aluminum and potassium sulfate (considered among the aluminum salts).
Solution of potassium arsenite (considered among the arsenic salts).

In going over the preparations of each metal we can usually note a certain salt of the metal that is used in making the other salts of the same metal. Thus, with the alkalis the carbonates are the salts usually employed. The salt thus selected as a "stock salt" is chosen for the most practical reasons. Among the deciding factors, cheapness and easy decomposition are the most important. Thus, with the alkalis, the chlorides are the most abundant salts, but since they are not easily decomposed, they are converted into carbonates, which are generally used. But besides these two factors other considerations come into play. Thus, in making potassium compounds the carbonate itself is not usually employed, because it is rather deliquescent and difficult to purify, therefore the bicarbonate, which occurs in handsome crystals, is selected. Hence, mere cheapness is not the absolute guide in the choice of material, but utility, average purity, and ease of action are among the other factors considered.

POTASSII HYDROXIDUM—Potassium Hydroxide

(Pot. Hydrox.—Caustic Potash)

KOH. Molecular weight, 56.10

Potassium Hydroxide contains not less than 85 per cent of total alkali, calculated as KOH, of which not more than 3.5 per cent is K_2CO_3.

Great caution is necessary in handling potassium hydroxide, as it rapidly destroys organic tissues.

Storage.—Preserve in air-tight containers. If bottles are used they must be of hard glass, and cork stoppers must be paraffined.

Summarized Description.

White fused masses or brittle sticks; very caustic; deliquescent in air, absorbing both water and carbon dioxide; soluble in 0.9 part of water, 3 parts of alcohol, and about 3 parts of glycerin; strongly alkaline. For details see U.S.P., p. 303. For ***tests for identity***, for ***impurities*** (heavy metals, organic matter, insoluble matter) and for ***assay*** see U.S.P., p. 303.

Remarks.—The official chemical must contain at least 85 per cent potassium hydroxide, a 100 per cent specimen being almost impossible except when just solidified, as it rapidly absorbs water from the air.

Potassium hydroxide is usually made by the evaporation of a solution of potassa, the manufacture of which will be given below. Official potassium hydroxide usually comes into the market in the form of cylindric sticks, about ½ inch in diameter, these being made by melting the potassium hydroxide and pouring into molds. The fusion of the hydroxide is an operation which must be carefully conducted, as the molten mass makes a very painful burn.

Potassium hydroxide is very deliquescent, and therefore must be kept in well-stoppered bottles. It is a practice, on the first opening of a bottle of potassa, to seal it with a considerable quantity of wax, so that on opening at later periods an air-tight joint can be renewed by simply passing a hot spatula over the wax.

Potassium hydroxide is considerably used in chemical manufacturing, as will be noted in the following pages. Medicinally, potassium hydroxide is used externally as a caustic, the official sticks being brought in direct contact with the surface desired to be burned. Its action, however, is so severe that in modern medicine its use is comparatively rare. The internal administration of potassium hydroxide is always in the form of a diluted solution.

It will be noted that the present Pharmacopœia calls this compound "potassium hydroxide," and not potassium hydrate, the same rule being true of all metallic hydrates. (See Sodium Hydroxide, Ferric Hydroxide, etc.) This is in line with the modern chemical nomenclature, which attempts to limit the word hydrate to water of crystallization. (See p. 173.)

Lye is supposedly crude potassium hydroxide, although much of the commercial lye is sodium hydroxide. While not as pure as the official variety, it is frequently stronger than 85 per cent.

Liquor Potassii Hydroxidi (U.S.P. X; N.F. VI) or *solution of potassium hydroxide* contains in each 100 cc. not less than 4.5 Gm. nor more than 5.5 Gm. of total alkali, calculated as KOH. It is made by dissolving 60 Gm. of 85 per cent potassium hydroxide in enough distilled water to make 100 cc. This preparation, commonly called *solution of potassa,* is now directed to be made by the simple solution of stick caustic potash in water. The recipe of the U.S.P. 1890 consisted of a double decomposition between potassium bicarbonate and calcium hydroxide, as shown in the following equation:

$$KHCO_3 + Ca(OH)_2 = CaCO_3 + KOH + H_2O.$$

Let us make this, if possible, still clearer by graphic expression:

Potassium bicarbonate		*Calcium hydrate*		
K		OH		KOH Potassium hydrate.
H	+	OH	=	HOH Water.
CO_3		Ca		$CaCO_3$ Calcium carbonate.
$KHCO_3$		$Ca(OH)_2$		

Note that in figuring out these processes it is the practical, rather than the theoretic, side that is considered. The compounds used are always the cheapest that will answer satisfactorily. Thus in the process just given, magnesium hydroxide could be used just as well as that of calcium, but it is not so employed merely because it is no better for the purpose than slaked lime and it costs much more.

It will be noticed that the calcium is removed in the form of an insoluble calcium compound, leaving nothing in solution but potassium hydroxide, provided that the proper molecular proportions are employed.

Solution of potassium hydroxide is a colorless liquid, having a very acrid caustic taste, and strongly alkaline reaction. It is so strongly alkaline that it attacks the glass of the bottles in which it is kept, forming therein a precipitate of potassium silicate. For the same reason it causes the glass stopper to adhere to the neck of the bottle. Therefore, if the solution is kept in glass-stoppered bottles, the stoppers should be protected by being smeared with petrolatum.

For the purposes of the practical pharmacist the method of manufacture of the present Formulary is better than the chemical process given above, as large quantities of the solution of potassium hydroxide should not be kept on hand, owing to the fact that it rapidly deteriorates in strength, and the present official process affords an easy method of making up small quantities.

Solution of potassium hydroxide is used as an antacid.

Dose.—1 cc. (15 minims) largely diluted in water.

In cases of poisoning by potassium hydroxide or its solution the antidote is that used for all caustic alkalis, namely, a mild acid, such as vinegar or lemon juice.

Note that *potassium* and *potassa* are not the same. Potassium is the element—the light alkali metal of the symbol K. Potassa, or caustic potash, is the hydroxide of potassium, its formula being KOH. Abandon the antiquated habit of saying "chlorate of potash," "carbonate of potash," and so on. Say "potassium chlorate," or "potassium carbonate," and thus have labels printed, gradually educating the public. The question of label printing deserves more time than is usually given it. We take the labels as the printer sees fit to spell them, because, forsooth! they are cheap.

Shop labels should follow pharmacopœial changes, and in so doing it is best to have both the old and the new names on the label, as suggested below: for some conservative people would be suspicious were only the new name on the label. The suggested label is as follows:

POTASSIUM CHLORATE.

(Chlorate of Potash.)

POTASSA SULFURATA—Sulfurated Potash
(Pot. Sulfurat.)

Sulfurated Potash is a mixture composed chiefly of potassium polysulfides and potassium thiosulfate and contains not less than 12.8 per cent of sulfur in combination as sulfide.

Storage.—Preserve in air-tight containers.

Summarized Description.

Irregular pieces; liver-brown, greenish-yellow or gray according to age; unstable; odor of hydrogen sulfide; soluble in about 2 cc. of water. For details see U.S.P., p. 295.

For *tests for identity*, and for *assay*, see U.S.P., p. 295.

Remarks.—This product is made by heating together potassium carbonate and sublimed sulfur in a covered crucible until the mass is in a state of perfect fusion.

A solution of sulfurated potassa may be made by boiling 3 Gm. of sublimed sulfur with 50 cc. of solution of potassium hydroxide.

According to the proportional quantities of the ingredients, and also the amount of heat employed, any of the following reactions may occur:

I. $3K_2CO_3 + 6S_2 = 2K_2S_5 + K_2S_2O_3 + 3CO_2$.
II. $3K_2CO_3 + 4S_2 = 2K_2S_3 + K_2S_2O_3 + 3CO_2$.
III. $4K_2CO_3 + 5S_2 = 3K_2S_3 + K_2SO_4 + 4CO_2$.

This shows that sulfurated potassa is not a definite chemical, but a mixture of the polysulfides, the sulfate, and the thiosulfate of potassium.

Sulfurated potassa, when freshly prepared, is in the form of irregular pieces, of a liver-brown color, and from the last fact it has been given the synonym *liver of sulfur.* On exposure to air, however, it absorbs moisture, oxygen, and carbon dioxide, changes to greenish yellow, and eventually to a gray mass, the latter consisting of potassium carbonate, thiosulfate, and sulfate. It is needless to say that only the liver-colored preparation should be dispensed, and this necessity renders the preparation ineligible. The manufacture of it by the retail pharmacist is a matter of considerable difficulty and uncertainty, and yet if purchased in pound lots from the manufacturer, it becomes useless, or almost so, before a quarter has been used; moreover, there is no satisfactory method of preserving it.

Sulfurated potassa is sometimes used under the name of potassium sulfide as a laxative, in 5-grain doses.

POTASSII ACETAS—Potassium Acetate

(Pot. Acet.)

$KC_2H_3O_2$. Molecular weight, 98.12

Potassium Acetate, when dried to constant weight at 150° C., contains not less than 99 per cent of $CH_3.COOK$.

Storage.—Preserve in air-tight containers.

Summarized Description.

White powder or satiny crystalline masses; very deliquescent; soluble in 0.5 part of water and in about 2 parts of alcohol. For details see U.S.P., p. 296.

For *tests for identity,* for *impurities* (heavy metals, arsenic) and for *assay* see U.S.P., p. 296.

Remarks.—This salt is made by the treatment of potassium bicarbonate with acetic acid, as shown in the following equation:

$$KHCO_3 + HC_2H_3O_2 = KC_2H_3O_2 + CO_2 + H_2O.$$

The potassium acetate remains in the solution, while the carbon dioxide escapes in gaseous form, with copious effervescence. The solution of potassium acetate is then evaporated to dryness on a water bath and immediately bottled.

Potassium acetate appears in the form of granules, odorless, and having a warm, saline taste. It is an extremely deliquescent salt, hence must always be kept in dry containers which are well sealed. It is given as a refrigerant and mild laxative.

Dose.—1 Gm. (15 grains).

Potassium arsenite, K_2HAsO_3, or $KAsO_2$, is official in the form of *Fowler's solution, liquor potassii arsenitis* (U.S.P.). This preparation will be discussed among the arsenical compounds.

POTASSII BICARBONAS—Potassium Bicarbonate

(Pot. Bicarb.)

$KHCO_3$. Molecular weight, 100.10

Potassium Bicarbonate, when dried to constant weight over sulfuric acid, contains not less than 99 per cent of $KHCO_3$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless monoclinic prisms or white granular powder; soluble in 2.8 parts of water; almost insoluble in alcohol. For details see U.S.P., p. 296.

For *tests for identity*, for *impurities* (excess of carbonate, heavy metals) and for *assay* see U.S.P., p. 296.

Remarks.—This salt is made by exposing the carbonate to the action of carbonic acid gas.

In expressing the reaction by simple addition, it is easy to see why the product is called *bi*carbonate.

The reaction is:

Potassium carbonate	K_2CO_3
Plus carbonic acid	H_2CO_3
Equals	$K_2H_2(CO_3)_2$
or two molecules of potassium bicarbonate	$2KHCO_3$

This shows that the bicarbonate really does contain twice as much carbonic acid as does the normal carbonate, a fact that is true of all salts bearing the prefix "bi."

Formerly the process of carbonation was carried on, suspending the carbonate in sacks over the fermenting vats of a brewery, and the crude bicarbonate thus obtained was placed on the market under the name of *saleratus*. Today (1935) upon calls for saleratus sodium bicarbonate is usually dispensed. At present the demand for saleratus is not large, and the carbonating is performed with carbon dioxide obtained from other sources, the resulting bicarbonate being purified by crystallization.

So many of our pharmaceutic chemicals depend upon water for their crystalline form that it is well to call attention to the fact that water is not essential in the formation of all crystals, potassium bicarbonate being an illustration of a chemical in well-defined crystals containing no water.

Potassium bicarbonate is an antacid. It is not often administered, its chief use being for the manufacture of other potassium compounds, as explained above. It might be noted that it is used as a carbonating agent in the manufacture of the solution of magnesium citrate.

Dose.—1 Gm. (15 grains).

POTASSII BITARTRAS—Potassium Bitartrate

(Pot. Bitart.—Cream of Tartar, Acid Potassium Tartrate)

$KHC_4H_4O_6$. Molecular weight, 188.14

Potassium Bitartrate, when dried to constant weight at 100° C., contains not less than 99.5 per cent of KOOC.CHOH.CHOH.COOH.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless opaque, rhombic prisms or white powder; odorless; acidulous taste; soluble in 162 parts of water and in about 7100 parts of alcohol. For details see U.S.P., p. 297.

For *tests for identity*, for *impurities* (insoluble matter; heavy metals, ammonia, alum and lead) and for *assay* see U.S.P., p. 298.

Remarks.—Potassium bitartrate (or *cream of tartar*) is the acid salt of tartaric acid $H_2C_4H_4O_6$, as explained on p. 400. It occurs in the form of a white, gritty powder and is also seen in the form of small rhombic crystals, although this form is comparatively rare. Its manufacture from argols will be discussed under tartaric acid. It is the one official potassium compound which is sparingly soluble in water, 1 part requiring

162 parts of water at 25° C. to dissolve it. The sparing solubility of cream of tartar is utilized in the manufacture of hydrobromic and other acids by the precipitation process. (See p. 454.) The fact just stated, however, that it does sparingly dissolve in water, shows us that hydrobromic acid made by the Fothergill process will be contaminated with bitartrate.

Cream of tartar is one of the most popular refrigerants and laxatives, being esteemed for sluggishness of the blood occurring during the spring and summer in warm climates. In such cases it is frequently administered in the form of lemonade, being combined with sugar and water, and possibly tamarinds, and the mixture taken in doses ranging from a wineglass to a cupful. Cream of tartar is a constituent of *compound jalap powder* (N.F. VI).

Dose.—2 Gm. (30 grains).

POTASSII BROMIDUM—Potassium Bromide
(Pot. Brom.)

KBr. Molecular weight, 119.01

Potassium Bromide, when dried to constant weight at 100° C., contains not less than 99 per cent of KBr.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless, cubical crystals or white granular powder; odorless; saline taste; soluble in 1.5 parts of water, in 200 parts of alcohol, and about 5.8 parts of glycerin. For details see U.S.P., p. 298.

For *tests for identity*, for *impurities* (bromate, iodides, heavy metals, sulfates, barium, excess of alkali, and for *assay* see U.S.P., p. 298.

Remarks.—This valuable salt is prepared in two ways: The first process is the formation of ferrous bromide from iron and bromine, and the decomposition of this ferrous bromide by treatment with potassium carbonate, the two reactions being as follows:

I.	Fe Iron.	+	Br_2 Bromine.	=	$FeBr_2$ Ferrous bromide.		
II.	$FeBr_2$ Ferrous bromide	+	K_2CO_3 Potassium carbonate.	=	$FeCO_3$ Ferrous carbonate.	+	$2KBr$ Potassium bromide.

The double decomposition between ferrous bromide and potassium carbonate works admirably, as the insoluble ferrous carbonate precipitates, leaving only potassium bromide in solution. This is filtered and the bromide crystallized out.

In actual practice the iron bromide Fe_3Br_8 is usually employed; that is a ferrous bromide solution containing an excess of bromine.

The second process is a little more complicated, but highly instructive. In the first stage, potassium hydroxide is treated with bromine, thus:

$$6KOH + 6Br = 5KBr + KBrO_3 + 3H_2O.$$

We get potassium bromide, KBr, contaminated with potassium bromate, $KBrO_3$, which is a salt of bromic acid, $HBrO_3$, which is derived from bromic oxide, Br_2O_5, in which compound bromine shows the valence v.

Bromic oxide	Br_2O_5
Plus water	$H_2\ O$
Equal	$H_2Br_2O_6$
or two molecules of bromic acid	$2H\ Br\ O_3$

This bromate is an undesirable addition to the bromide, and must be converted into the latter. If we compare the formula of the bromide, KBr, with that of the bromate, $KBrO_3$, we find the latter differs from the former only by having oxygen. This oxygen must be removed, and this is accomplished by the process of reduction, the reducing agent employed being carbon or charcoal, just as in the manufacture of sulfurous acid, the reaction being as follows:

$$KBrO_3 + C_3 = KBr + 3CO.$$

Therefore summarizing this method of making potassium bromide, potassium hydroxide is treated with bromine, the solution is evaporated to dryness, the residue is heated to redness with charcoal,' the cooled charred mass is treated with water, the filtrate is evaporated until crystals of the bromide separate out.

Potassium bromide is used as a sedative and nervine, and is frequently administered in combination with chloral.

Dose.—1 Gm. (15 grains).

POTASSII CARBONAS—Potassium Carbonate (Pot. Carb.)

K_2CO_3. Molecular weight, 138.19

Potassium Carbonate, when dried to constant weight at 180° C., contains not less than 99 per cent of K_2CO_3. It contains not less than 10 per cent and not more than 15 per cent of water.

Storage.—Preserve in air-tight containers.

Summarized Description.

White granular deliquescent powder; soluble in 0.9 part of water; insoluble in alcohol. For details see U.S.P., p. 299.

For *tests for identity*, for *impurities* (insoluble matter, heavy metals; arsenic) and for *assay* see U.S.P., p. 299.

Remarks.—Potassium carbonate is known by several synonyms, among others, *salt of tartar*. It is called this because it can be made by heating cream of tartar, the reaction being:

$$2KHC_4H_4O_6 + 5O_2 = K_2CO_3 + 7CO_2 + 5H_2O.$$

The other synonyms are *pearl ash*, and *salt of wormwood*, the latter name being derived from the fact that a variety of potassium carbonate, which was well esteemed some centuries ago, was made from the ashes of wormwood.

As already mentioned (p. 459), potassium carbonate is one of the chief sources of the element, and large quantities of the crude salt are obtained from suint and from ashes. At the same time, however, considerable is manufactured by the same process used in sodium carbonate, and this process will be considered under making sodium carbonate (p. 483).

Potassium carbonate is a white, granular powder; it is quite deliquescent, and hence should, like potassium acetate, be kept in well-stoppered bottles. It is used as an antacid, although its action is rather too irritating for general use, sodium bicarbonate being preferred. Taken in large quantities it has caustic action, and as an antidote, a mild acid should be used.

Potassium carbonate is used considerably in some sections as an alkaline hair-wash, the object being to prevent blond hair from turning dark. For this purpose it is of little value, and is, moreover, decidedly detrimental to the health of the hair.

Dose.—1 Gm. (15 grains).

POTASSII CHLORAS—Potassium Chlorate

(Pot. Chloras)

$KClO_3$. Molecular weight, 122.55

Potassium Chlorate contains not less than 99 per cent of $KClO_3$.

Great caution should be observed in handling this salt, as dangerous explosions are liable to occur when it is heated or subjected to concussion or to trituration with organic substances, such as cork, tannic acid, dust, sucrose, etc., or with charcoal, sulfur, sulfides, hypophosphites, reduced iron, or other easily oxidizable substances.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless monoclinic prisms or plates or white granular powder; soluble in about 16.5 parts of water; insoluble in alcohol. For details see U.S.P., p. 299.

For *tests for identity*, for *impurities* (heavy metals) and for *assay* see U.S.P., p. 299.

Remarks.—The formula of potassium chlorate is $KClO_3$, from chloric acid, $HClO_3$, from chloric oxide, Cl_2O_5, the graphic formula of which was given on p. 388.

The formula of potassium chlorate, $KClO_3$, is analogous to $KBrO_3$, potassium bromate, and the chlorate can be made by passing chlorine into potassium hydroxide by a reaction similar to that occurring in the manufacture of potassium bromide:

$$6KOH + 6Cl = 5KCl + KClO_3 + 3H_2O.$$

But by this method, from 6 molecules of potassium hydroxide only 1 molecule of potassium chlorate is obtained, the remaining 5 atoms of potassium going to waste as potassium chloride, and a better method of manufacture therefore is from chlorinated lime. This body, on being boiled with water, decomposes into calcium chloride and calcium chlorate by the following reaction:

$$3Ca(OCl)_2 + \text{heat} = Ca(ClO_3)_2 + 2CaCl_2.$$

The calcium chlorate solution is then treated with potassium chloride, when the following reaction occurs:

$$Ca(ClO_3)_2 + 2KCl = CaCl_2 + 2KClO_3.$$

The resulting calcium chloride is very soluble in water, and remains in solution, while the sparingly soluble potassium chlorate crystallizes out.

Practically all commercial potassium chlorate is now made by the electrolysis of potassium chloride resulting in the following series of reactions:

(*a*) $H_2O + \text{electricity} = H_2 + O$.
(*b*) $KCl + H_2O + \text{electricity} = KOH + Cl + H_2$.
(*c*) $KOH + Cl_2 = KOCl + KCl + H_2O$.
(*d*) $KOCl + O_2 = KClO_3$.
(*e*) $3KOCl = KClO_3 + 2KCl$.

The solubility of potassium chlorate is worth more than passing notice. U.S.P. IX erroneously stated that 1 Gm. of the salt would dissolve in 11.5 cc. of water at 25° C. U.S.P. X more correctly states that 1 Gm. dissolves in 16.5 cc. of water at 25° C. It is the custom of many drug stores to keep on hand a stock solution of potassium chlorate which is labeled ½ drachm to the fluidounce. If by ½ drachm 30 grains is intended, such a solution is impossible at ordinary temperatures, inasmuch as only 27 grains of the salt will dissolve in an ounce of cold water.

Nor is it wise for the operator to try to coax the remaining potassium chlorate to go into solution by warming the mixture. A solution will ensue, but on cooling the excess will surely separate out. Physicians, not aware of the exact solubility, sometimes prescribe 30 grains of potassium chlorate to the ounce of solution, and intend same for gargle. If this prescription is dispensed with the excess of the salt remaining in the mixture, the undissolved salt will act as irritant to the inflamed mucous membrane which it is intended to relieve. Hence the careful pharmacist always dispenses a clear, filtered solution of potassium chlorate when intended for gargle.

Potassium chlorate is a powerful oxidizing agent, and for this reason combines with many easily oxidizable substances, such as sulfur, antimony sulfide, phosphorus, starch, sugar, so energetically as to produce explosions; hence the pharmacopœial warning that this salt should not be triturated with any of the above substances. When called upon to mix such substances as potassium chlorate and sugar, they should first be powdered separately and then mixed together with a bone spatula on a piece of paper.

Potassium chlorate is a mild antiseptic, this property being due to its oxidizing action. Its chief application for this purpose is in cases of sore throat, for which it is much esteemed. Its indiscriminate use, however, for this purpose, especially in the form of lozenges and compressed tablets, is not advisable, for investigation shows that it has an irritating action on the bladder, and therefore should not be swallowed in large quantities. It is now being used in tooth pastes on the theory that it exerts a bleaching effect as well as a cleansing and deodorant action.

Dose (U.S.P. X).—250 mg. (4 grains).

POTASSII CITRAS—Potassium Citrate

(Pot. Cit.)

$K_3C_6H_5O_7.H_2O$. Molecular weight, 324.34

Potassium Citrate [$C_3H_4.OH.(COOK)_3.H_2O$], when rendered anhydrous by drying at 150° C., contains not less than 99 per cent of $C_3H_4.OH.(COOK)_3$. It contains not less than 3 per cent and not more than 6 per cent of water.

Storage.—Preserve in air-tight containers.

Summarized Description.

Transparent prismatic crystals or white granular powder; somewhat deliquescent; soluble in 1 part of water; almost insoluble in alcohol. For details see U.S.P., p. 300.

For *tests for identity*, for *impurities* (heavy metals, arsenic, lead and tartrate) and for *assay* see U.S.P., p. 300.

Remarks.—This salt is made by treatment of potassium bicarbonate with citric acid, as shown in the following equation:

$$3KHCO_3 + H_3C_6H_5O_7 = K_3C_6H_5O_7 + 3CO_2 + 3H_2O.$$

As mentioned above, the bicarbonate is used in preference to the carbonates in the manufacture of most of the potassium salts, and in this case the bicarbonate is absolutely necessary, the citrate made from the carbonate being quite unsatisfactory.

The potassium citrate occurs in transparent prismatic crystals or in white granular powder, both forms being rather deliquescent. It is used as a refrigerant.

Dose.—1 Gm. (15 grains).

POTASSII CITRAS EFFERVESCENS—Effervescent Potassium Citrate (Pot. Cit. Eff.)

Condensed Recipe.

Ingredients.—Potassium citrate, 200 Gm.; sodium bicarbonate, 477 Gm.; tartaric acid, 252 Gm.; uneffloresced citric acid, 162 Gm.

Manipulation.—After drying the citrate on a water bath mix it with the acids and then with the bicarbonate. Granulate the mixture by heating to between 93° and 104° C. on glass plates in an oven and when soft, rub the mass through coarse No. 6 sieve. Then dry and seal in tight containers. For details see U.S.P., p. 301.

Remarks.—The granular effervescent salts have been considered on p. 327, so here it suffices to say that this preparation is supposed to contain the acids and the potassium bicarbonate in uncombined form, but that when mixed with water, the chemicals combine, with liberation of carbon dioxide gas and copious effervescence, making the mixture more palatable.

Dose.—4 Gm. (60 grains).

Liquor Potassii Citratis (N.F. VI) or *solution of potassium citrate* is an aqueous solution of potassium citrate. It is made by dissolving separate solutions of potassium bicarbonate and citric acid, the quantity of the chemicals in each being so adjusted that when equal volumes of the two solutions are mixed, slightly acidulated potassium citrate will result. It is assumed that the pharmacist will not blend the two solutions until an order for the finished solution is received, and in this way the solution will be dispensed with sufficient effervescence remaining to make the liquid more palatable. The exact amount of "sparkle" is a matter of pharmaceutic judgment, for if the mixed liquid is quickly poured into a bottle and is tightly corked, there is danger of sufficient gas being evolved to cause an explosion of the flask in the hands of the purchaser.

The Pharmacopœia of 1890 gave as a synonym of this solution *mistura potassii citratis,* because this preparation is intended to replace the mixture of potassium citrate (*neutral mixture*) of the Pharmacopœia of 1880. The product of 1880 was much more palatable than the present official solution, because instead of citric acid, fresh lemon juice was employed.

Potassium citrate is a mild refrigerant, and when dispensed in the effervescent form, constitutes a refreshing draft for fever patients.

A modification of the preparation quite popular in French countries is *potion de Riviere.* The French Codex directs that this be made by preparing two solutions, one consisting of citric acid, 2 parts; water, 50 parts; syrup of lemon, 15 parts; the other consisting of sodium bicarbonate, 2 parts; water, 50 parts; syrup, 15 parts, dispensing the two solutions in separate bottles, with directions to patient to mix equal parts and drink while effervescing. A similar recipe is found in the National Formulary. (See p. 214.) The original potion de Riviere was a solution of potassium citrate. *Dose.*—Of official solution: 15 cc. (4 fluidrachms).

POTASSII ET SODII TARTRAS—Potassium and Sodium Tartrate (Pot. et Sod. Tart.—Rochelle Salt)

$KNaC_4H_4O_6.4H_2O$. Molecular weight, 282.19

Potassium and Sodium Tartrate' ($KOOC.CHOH.CHOH.COONa.4H_2O$), when rendered anhydrous by drying at 150° C., contains not less than 99 per cent of $KOOC.CHOH.CHOH.COONa$. It contains not less than 21 per cent and not more than 26 per cent of water.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless rhombic prisms or white powder; somewhat efflorescent; soluble in 0.9 part of water; almost insoluble in alcohol. For details see U.S.P., p. 302.

For *tests for identity,* for *impurities* (heavy metals, ammonia, lead) and for *assay* see U.S.P., p. 302.

Remarks.—This compound is interesting as one of the two official double salts of tartaric acid, the other being tartar emetic. (See p. 586.) It is made by treating potassium bitartrate with sodium bicarbonate, when the following reaction will occur:

$$KHC_4H_4O_6 + NaHCO_3 = KNaC_4H_4O_6 + CO_2 + H_2O.$$

The chemistry of this body can be discussed when the composition of the acid from which it is derived is noticed; hence it is reserved until later (p. 685).

Sodium and potassium tartrate (*Rochelle salt*, *sal Seignette* or *sal polychresticum*) is used as a mild laxative and refrigerant. It is one of the constituents of official Seidlitz powder.

Dose.—10 Gm. (2½ drachms).

POTASSII IODIDUM—Potassium Iodide
(Pot. Iodid.)

Symbol, KI. Molecular weight, 166.02

Potassium Iodide, when dried to constant weight at 100° C., contains not less than 99 per cent of KI.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless or white cubic crystals or white granular powder; pungent, saline, bitter taste; soluble in 0.7 part of water and about 17 parts of alcohol. For details see U.S.P., p. 304.

For *tests for identity*, for *impurities* (iodate, heavy metals, barium, cyanide, nitrate, nitrite, ammonia, thiosulfate, alkali) and for *assay* see U.S.P., p. 304.

The manufacture of this important chemical is similar to that of potassium bromide, only the first process is by treatment of ferric iodide with potassium bicarbonate or carbonate. This is somewhat different from the ferrous bromide reaction in making potassium bromide. As in the bromide process, iron is treated with the halogen element, making the ferrous iodide solution; however, more iodine is added, making the more stable ferric iodide, FeI_3, and when this is treated with potassium carbonate, the following reaction occurs:

$$2FeI_3 + 3K_2CO_3 + 3H_2O = 6KI + 3CO_2 + 2Fe(OH)_3.$$

The second process is by treating solution of potassium hydroxide, and is closely similar to that for making potassium bromide:

$$6KOH + 6I = 5KI + KIO_3 + 3H_2O.$$

As in the bromide process, the iodate is reduced to iodide by heating with charcoal, viz.: $KIO_3 + C_3 = KI + 3CO.$

Potassium iodide occurs in colorless, translucent, cubic crystals, having a faint iodine odor, and a saline, afterward bitter, taste. It is exceedingly soluble in water (1 part to 0.7 at 25° C.), which renders possible the preparation of the saturated solution of potassium iodide, containing 456 grains of chemical in a fluidounce of the finished solution. (For Solution of Potassium Iodide, N.F., see p. 214.)

As mentioned above, the crystals of potassium iodide should be either transparent or else translucent. The larger majority of the commercial iodide is in white, opaque crystals. These are impure, being crystallized from an alkaline medium. It is but fair to the manufacturer, however, to say that the preparation of a neutral potassium iodide is a matter of considerable difficulty, as there is danger of the separation of the iodine turning the crystals brownish.

Potassium iodide is a most valuable alterative. It is a constituent of *compound solution of iodine, tincture of iodine, mild tincture of iodine* and *ointment of iodine.*

Dose.—300 mg. (5 grains).

Antiluetic—2 Gm. (30 grains).

POTASSII NITRAS—Potassium Nitrate

(Pot. Nitras—Saltpetre)

KNO_3. Molecular weight, 101.10

Potassium Nitrate, when dried to constant weight at 100° C., contains not less than 99 per cent of KNO_3.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless rhombic prisms or white crystalline powder; saline and cooling taste; slightly hygroscopic, soluble in about 2.8 parts of water and about 500 parts of alcohol. For details see U.S.P., p. 305.

For *tests for identity,* for *impurities* (heavy metals, chloride, chlorate) see U.S.P., p. 305.

Remarks.—This chemical, commonly called *saltpetre,* has been in popular use for centuries. The original method of manufacture was interesting; being made by the treatment of ashes with decaying nitrogenous matter, such as manure and cattle urine. The mass was allowed to stand under roughly constructed sheds for several months, being occasionally turned so as to present new surfaces to the air. When the fermentation of the mass is completed, it is placed in crude percolators and lixiviated with water, whereby the finished potassium nitrate is separated from the extraneous matter.

Repeated crystallization of this solution eventually results in a pure crystalline nitrate.

Investigations of the manufacture of saltpetre on these "saltpetre plantations" has shown that the change of the nitrogenous matter to the nitrate is a species of fermentation, being produced by a peculiar microscopic plant called *nitromonas.* This process of saltpetre manufacture was formerly largely used, as it yielded not only all the saltpetre used, but also because this potassium nitrate was the source of nitric acid and all the nitrates.

At present, however, the main source of nitric acid is Chile saltpetre (see p. 426), from which potassium nitrate is made, as shown in the following equation:

$$NaNO_3 + KCl = KNO_3 + NaCl.$$

the resulting salts being separated by fractional crystallization. It is also made from synthetic sodium nitrate by a similar process. (See p. 446.)

One of the largest general uses of potassium nitrate is in the manufacture of *gunpowder,* of which the average formula is potassium nitrate, 75 parts; powdered charcoal, 15 parts; and sulfur, 10 parts, the mass being mixed together, then granulated by wetting the mass, passing it through a sieve, and carefully drying the resulting granules. Gunpowder explodes by the following reaction:

$$2KNO_3 + S + 3C = K_2S + 3CO_2 + N_2.$$

On examination of the above equation it will be seen that the chemical action between the three solids results in the formation of two gases and a comparatively small amount of the solid potassium sulfide. In addition to the liberation of these gases, the reaction produces much heat causing a sudden expansion of the surrounding air, which is the main cause of the explosion. In fact, the modern definition of an explosive is a body capable of undergoing rapid reaction with the evolution of heat and the development of large volume of gas.

In the potassium sulfide of the above reaction is found an explanation of the peculiar odor of a burned fire-cracker.

In medicine, potassium nitrate is used largely as a diuretic.

Sal Prunelle is an old-time form of potassium nitrate made by fusing the salt at low temperature and then pouring into spherical molds.

Dose.—300 mg. (5 grains).

POTASSII PERMANGANAS—Potassium Permanganate (Pot. Permang.)

$KMnO_4$. Molecular weight, 158.03

Potassium Permanganate, when dried to constant weight over sulfuric acid, contains not less than 99 per cent of $KMnO_4$.

Great caution should be observed in handling potassium permanganate, as dangerous explosions are liable to occur when it is brought into contact with organic or other readily oxidizable substances, either in solution or in the dry condition.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

Slender, dark purple, monoclinic prisms; sweet, then disagreeable astringent taste; soluble in 14.2 parts of water; decomposed by alcohol; dissociates on heating into oxygen, potassium manganate and manganese dioxide. For details see U.S.P., p. 306.

For *tests for identity* and for *assay* see U.S.P., p. 306.

Remarks.—Potassium permanganate is now given the formula $KMnO_4$, in preference to that of the Pharmacopœia of 1880, $K_2Mn_2O_8$. It represents the highest known valence of manganese—the valence VII—and is an analogue of potassium perchlorate, $KClO_4$, which comes from perchloric oxide, Cl_2O_7, the graphic formula of which was given on p. 388. The permanganate is one of the oxidizing agents, the action of which is explained on p. 447.

It is made by treatment of manganese dioxide with potassium hydroxide and potassium chlorate, this mixture yielding potassium manganate, as shown in the following equation:

$$3MnO_2 + 6KOH + KClO_3 = 3K_2MnO_4 + KCl + 3H_2O.$$

It will be observed that potassium manganate (K_2MnO_4) has a formula similar to that of potassium sulfate, in this body the manganese acting with the valence VI. When this green potassium manganate is boiled with water, it is converted into the purple potassium permanganate, as shown in the following equation:

$$3K_2MnO_4 + 3H_2O = 2KMnO_4 + MnO_2 + 4KOH + H_2O.$$

In modern technic, this last reaction is performed by electrolysis.

The process occurs in miniature in an important test for manganese, which consists of fusing the three constituents above given on a piece of platinum foil and then boiling in water. If the fused mass is green and the resulting liquid is pink, it indicates the presence of manganese.

By reason of this change of tint, potassium permanganate has been given the synonym of *mineral chameleon.*

It will be noticed that the products of the final reaction consist of some manganese dioxide and also potassium hydroxide, and in order to secure the permanganate from this mixture, it is necessary to neutralize the excess of potassium hydroxide with sulfuric acid. The solution of permanganate is then filtered through asbestos to remove the precipitated manganese dioxide, and the filtrate concentrated until crystallization begins.

Potassium permanganate occurs in purple, monoclinic crystals, which possess a blue, metallic luster in reflected light. It is soluble in 14.2 parts of water and forms a purple-red solution. The Pharmacopœia gives a warning that it should never be triturated with easily oxidizable substances, while pills of potassium permanganate should not be made with ordinary excipients, but with petroleum mass (petrolatum and kaolin). Permanganate stains the skin, giving a brown color. This can be removed by washing with solutions of tartaric acid or sodium thiosulfate.

The oxidizing action of potassium permanganate in neutral solution is best shown by the following equation:

$$2KMnO_4 + H_2O = 2MnO_2 + 2KOH + O_3.$$

This, when reduced to words, means that 2 molecules of the permanganate yield 3 atoms of available oxygen. By comparison of this with the oxidizing equation of nitric acid, given on p. 447 it is seen that the reaction in the 2 cases is similar.

When permanganate acts in acid solution, 2 molecules (or 1 molecule of $K_2Mn_2O_8$ if that is accepted as the formula) liberate 5 atoms of oxygen, as shown in the following equation:

$$2KMnO_4 + 3H_2SO_4 = 2MnSO_4 + K_2SO_4 + 3H_2O + O_5.$$

This is the basis of the use of potassium permanganate in volumetric analysis (Part V).

Potassium permanganate is one of the most convenient oxidizing agents for use in organic chemistry. As already stated, nitric acid is the oxidizing agent generally used in the ordinary processes of oxidation we meet in pharmacy. The acid, however, acts too violently for use in many organic oxidations, and for such purposes either potassium permanganate or chromic acid is employed.

Potassium permanganate is a valuable antiseptic in medicine, and is largely used in surgical practice. One advantage it possesses over the ordinary oxidizing antiseptics is its comparative freedom from caustic action. In practice it is frequently prescribed in the form of *Condy's fluid*, which consists of 128 grains permanganate to 1 pint of distilled water. It is now largely used internally in a solution 1 : 1000 as an antidote for organic poisons.

Dose.—60 mg. (1 grain), preferably in a fine powder in capsules.

Potassa cum Calce (U.S.P. 1890; N.F. IV) represents the official potassa diluted with its own weight of freshly burned lime, the two being rubbed together in a warm iron mortar until a powder is formed. This preparation is supposed to be used as a caustic in preference to the pure potassa. It is never used internally.

Potassii Cyanidum (U.S.P. VIII), or *potassium cyanide* (KCN) is made by heating potassium ferrocyanide with potassium carbonate in a red-hot crucible, when the following reaction ensues:

$$K_4Fe(CN)_6 + K_2CO_3 = 5KCN + KOCN + CO_2 + Fe.$$

It will be seen from this reaction that the product will be contaminated with potassium cyanate, KOCN (p. 753). If a perfectly pure product is desired, it is made by passing hydrocyanic acid gas into an alcoholic solution of potassium hydroxide.

Potassium cyanide is now being made by an electric process. The demand for this chemical has greatly increased in late years, it being very largely used in metallurgic processes, the extraction of gold and silver from ores, etc.

Potassium cyanide occurs in white, irregular lumps, or as a white, granular powder, usually exhaling the odor of hydrocyanic acid, though odorless when perfectly dry. It is rather deliquescent, and therefore should be kept in well-stoppered bottles.

Great care should be taken in handling potassium cyanide, since it is a deadly poison.

When boiled with water, potassium cyanide splits into up potassium formate (p. 651) and ammonia, as shown in the following equation:

$$KCN + 2H_2O = KCHO_2 + NH_3.$$

For this reason solutions of the cyanide should never be heated.

In medicine, potassium cyanide affords a convenient way of obtaining the medicinal action of hydrocyanic acid, and a prescription calling for potassium cyanide and citric acid was formerly considerably used. *Dose.*—10 mg. (⅕ grain).

Potassii Dichromas (U.S.P. VIII) or *potassium dichromate*, is an interesting chemical inasmuch as it contains no hydrogen whatever, and in this case the rule laid down, that an acid salt is one in which all the hydrogen of the acid is not replaced by a metal, fails utterly. It is just such exceptions and variations in the nomenclature of chemistry that make its study difficult.

Let us dissect this compound, potassium dichromate, $K_2Cr_2O_7$. Its sister compound is potassium chromate, K_2CrO_4, which is derived from chromic acid, H_2CrO_4, which comes from chromic oxide, CrO_3, a body analogous to SO_3.

Potassium chromate	K_2CrO_4
Plus chromic oxide	CrO_3
Gives potassium dichromate	$K_2Cr_2O_7$

This compound is made from chromic iron ore, a mineral formerly mined in considerable quantities in Pennsylvania and Maryland, but now practically all imported from Europe. This ore is roasted with potassium carbonate and lime in presence of air, when the potassium chromate is formed by the following reaction:

$$2FeOCr_2O_3 + CaO + 3K_2CO_3 + 7\ O\ (\text{from air}) = 3K_2CrO_4 + CaCrO_4 + Fe_2O_3 + 3CO_2.$$

This potassium chromate is then converted into potassium dichromate by treatment with sulfuric acid, as shown in the following equation:

$$2K_2CrO_4 + H_2SO_4 = K_2Cr_2O_7 + K_2SO_4 + H_2O.$$

The calcium chromate of the first reaction is treated with potassium sulfate, and is thus converted into potassium chromate, which is changed to dichromate by use of sulfuric acid.

Dichromate of potassium occurs in orange-yellow crystals, which are soluble in 9 parts of water and in 1½ parts of boiling water. Its chief use in pharmacy is as an oxidizing agent, for when treated with sulfuric acid it splits into chromic acid, one of the best oxidizing agents. It will be recalled that the oxidizing action of the dichromate mixture was suggested as a way of cleaning mortars. (See p. 136.) The dichromate mixture is also used as a battery fluid. It is rarely used in medicine; if so, it is employed as a remedy in syphilis.

If an excessive dose is taken, the antidote would be a mild alkali, such as soap, magnesia, or chalk. *Dose.*—10 mg. (⅕ grain).

Potassii Ferrocyanidum (U.S.P. VIII) $K_4Fe(CN)_6.3H_2O$ is interesting as the source of cyanides. It is made from a mixture of nitrogenous animal matter, pearl ash (potassium carbonate), and scrap iron, all being heated together in an iron pot.

Details of the manufacture of this substance will be studied when we consider the cyanogen preparations. (See p. 752.)

Potassium ferrocyanide is rarely used in medicine. When pure, it is not poisonous despite the presence of the cyanogen group. A solution of potassium ferrocyanide, we will find later, is used in testing iron (p. 556). *Dose.*—500 mg. (8 grains).

Under this head mention might be made of *potassium ferricyanide*, $K_3Fe(CN)_6$, which is used in testing for iron in the ferrous form (p. 556). The chemistry of both of these bodies is difficult and will be left to be discussed under the Cyanogen Compounds.

Potassii Hypophosphis (N.F. VI) or *potassium hypophosphite*, KPH_2O_2, is made by treating calcium hypophosphite with potassium carbonate, as shown in the following equation:

$$Ca(PH_2O_2)_2 + K_2CO_3 = 2KPH_2O_2 + CaCO_3.$$

Solution of potassium hypophosphite is removed from the insoluble calcium carbonate by filtration. The solution is then evaporated on a water bath with great care until a granular mass results. The caution as to evaporation is necessary in heating every hypophosphite, as even at the temperature of the water bath there is danger of an explosion, due to the formation of the spontaneously combustible phosphine, PH_3. The salt occurs in opaque hexagonal plates, in crystalline masses or in granular powder and is soluble in 0.6 part of water.

Potassium hypophosphite, in common with all hypophosphites, is used largely as a tonic in wasting diseases, and is a constituent of the *syrup of hypophosphites* (N.F.) and *compound syrup of hypophosphites* (N.F.). It is now considered of little therapeutic value. *Dose.*—500 mg. (8 grains).

Potassii Sulphas (N.F. VI) or *potassium sulfate*, K_2SO_4, is made from the ore, *kainite*, which has the composition of $K_2SO_4MgSO_4MgCl_2 5H_2O$. It is also produced by treating either potassium nitrate or potassium chloride with sulfuric acid. It is in the form of colorless, transparent, rhombic crystals, soluble in 10 parts of water. It is interesting to note that these crystals contain no water of crystallization, thereby differing from the otherwise similar sodium sulfate, which contains 10 molecules of water of crystallization.

Potassium sulfate is employed as a diuretic and refrigerant. Its use is rather limited, especially as the Pharmacopœia has discontinued its use in the manufacture of Dover's powder. The original recipe for this pharmaceutic directed that the ipecac and opium be triturated with crystallized potassium sulfate; but in the present Pharmacopœia sugar of milk is substituted for this salt. (See p. 316.) *Dose.*—1 Gm. (15 grains).

BIBLIOGRAPHY

Potassium.—(History) Thorpe, Ch. News, 97, 1908, 193 and 210; Lippmann, Ch. Zt., 32, 1908, 977; Witt, Ch. Zt., 32, 1908, 1029; Ostwald, Zt. angew. Ch., 21, 1908. Hackh, A.J.P., 10, 1918, 573; Dyson, Ph. Jl., 50, 1931, 580. (Sources) Zaragüeta, C.A., 7, 1913, 750; Green and Johnson, Ch. Eng., 15, 1912, 55; Langbeck, Jl. Soc. Ch. Ind., 9, 1890, 356; Greif, Ch. Zt., 14, 1890, 1440, 1504 and 1535; Mueller, Ph. Jl., [3], 2, 1872, 565. Berger Schw. Ap. Zt., 53, 1915, 90; Anon., Ch. News, 121, 1920, 250; Teeple, Jl. Ind. Eng. Ch., 15, 1923, 419; Laŭcks, C.A., 10, 1916, 1408; Anon., Can. Ch. Jl., through C.A., 11, 1917, 2719; Onslow, C.A., 24, 1930, 1185; Anon., Jl. Soc. Ch. Ind., 47, 1928, 341; Mushketov, Nat. Dr., 58, 1928, 170; Wolf and Yatlov, C.A., 23, 1929, 1220; Shtern and Levin, *ibid.*, 22, 1928, 4087; Anon., Jl. Soc. Ch. Ind., 48, 1929, 832; Cullen, *ibid.*, 52, 1931, 1058; Charrin, C.A., 26, 1932, 563. (American sources) Hart, Jl. Ind. Eng. Ch., 7, 1915, 670; Dolbear, Met. Ch. Eng., 13, 1915, 481; Anon., Yearbook, A.Ph.A., 6, 1917, 290; Cranfield and others, Yearbook A.Ph.A., 7, 1918, 351; Bateman, Ch. Met. Eng., 21, 1919, 615; Shreve, Jl. Ind. Eng. Ch , 14, 1922, 542; Teeple, Jl. Ind. Eng. Ch., 14, 1922, 787 and Jl. Soc. Ch. Ind., 46, 1927, 73, and 47, 1928, 345T.; Klein, Jl. Ind. Eng. Ch., 18, 1926, 1358; Turrentine and co-workers, *ibid.*, 17, 1925, 1177; Broughton and co-workers, C.A., 24, 1930, 4348; Robertson, Jl. Ind. Eng. Ch., 21, 1929, 520; Berliner, Bureau of Mines Bull., 327, 1930, 1–578; Storch, Jl. Ind. Eng. Ch., 22, 1930, 934; Hill and Adams, *ibid.*, 23, 1931, 658; Blanton, *ibid.*, News Ed., 22, 1930, 11. (Isolation) Brunner, Schweigger's Jl., 35, 1823, 517. Lorenz and Clark, Jl. Soc. Ch. Ind., 22, 1903, 561; Hare, A.J.P., 5, 1834, 237. (Properties) Richards and Brink, Jl. Am. Ch. Soc., 29, 1907, 117. (Tests) Lutz, Jl. Soc. Ch. Ind., 39, 1920, 584A.

Sodium Salts vs. Potassium Salts.—Anon., Ph. Jl., 93, 1914, 507.

Sulphurated Potassa.—(Composition) Packer, Bull. de pharm. sudest, 18, 1913, 576; Watts, Ph. Jl., [3], 1, 1870, 416. (Preparation) Foran, Proc. Pa. P.A., 45, 1922, 213. (Assay) Funke, Dr. Circ., 65, 1921, 468. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1156.

Cream of Tartar.—(History) Arny, Am. Dr., 39, 1901, 3. (Manufacture) Best, Met. Ch. Eng., 13, 1915, 613.

Potassium Bromide.—(Manufacture) Henry, Jl. de ph., 15, 1829, 54; Tilden, Ph. Jl., [3], 2, 1872, 683; Hüttner, C.A., 15, 1921, 3369 and 16, 1922, 4018. (Solubility) Germuth, Jl. Frank. Inst., 212, 1931, 343.

Potassium Carbonate.—(History) Wootton, 1, 1910, 372; Anon., Am. Dr., 67, 1919, 218. (Source) Bradley, Met. and Ch. Eng., 13, 1915, 841.

Saleratus.—Husa, Jl. A.Ph.A., 16, 1927, 59.

Potassium Chlorate.—(History) Anon., Jl. Soc. Ch. Ind., 42, 1923, 224. (Manufacture) Blumenberg, Am. Dr., 24, 1894, 273; Morin, Ann. Ch. Phys., through Gmelin Kraut, 2^1, 1906, 100, Liebig, Mag. Pharm., through Gmelin-Kraut, 2^1, 1906, 101. Thumm, Z. angew. Ch., 35, 1922, 433; Ilijinsky, Jl. Soc. Ch. Ind., 42, 1923, 1067A. Shraibman, C.A., 25, 1931, 4361; Stubinkov and Pupko, *ibid.*, 25, 1931, 5252. (Explosions) Anon., A.Ph.A., 57, 1909, 238; Rowland, Jl. Ind. Eng., Ch., 8, 1916, 517. (Uses) Bachson, Sch. Wsch. f. Ch., Ph., 57, 1913, 120. (Toxicity) Rosenbloom, C.A., 6, 1912, 2462; Ulrich and Shternov, Jl. Pharm. Exp. Therap., 34, 1928, 391.

Potassium Cyanide.—(History) Van Deventer, Ch. Week.bl, 25, 1928, 101. (Manufacture) Baup, Jl. de ph., 9, 1823, 37; Donovan, Ph. Jl., 2, 1843, 573; Liebig, A.J.P., 14, 1843, 295; Wöhler, A.J.P., 18, 1846, 271; Rodgers, F. and E., Phil. Mag., [3], 4, 91, through Thorpe's Dict., 2, 1912, 193. (Uses) Thompson, C.A., 25, 1931, 5121.

Neutral Mixture.—Scattergood, A.J.P., 5, 1834, 16.

Rochelle Salt.—(History) Anon., Ch. and Dr., 77, 1910, 611.

Potassium Ferrocyanide.—(Manufacture) Readman, Jl. Soc. Ch. Ind., 8, 1889, 757; Smith, A.J.P., 20, 1848, 170; Conroy, Jl. Soc. Ch. Ind., 15, 1896, 8; *ibid.*, 17, 1898, 98; Laming, A.J.P., 18, 1847, 277; Chemnitius, Jl. Soc. Ch. Ind., 47, 1928, 190B; Lange, C.A., 22, 1928, 3267.

Potassium Hypophosphite (Use) Anon., Jl. A.M.A., 62, 1914, 1346, and 74, 1920, 1661.

Potassium Iodide.—(Manufacture) Duhamel, A.J.P., 6, 1834, 110; Squire, Ph. Jl., [2], 8, 1862, 548; Henry, A.J.P., 1, 1829, 201. (Saturated solution) Lascoff, Dr. Circ., 57, 1913, 145.

Potassium Nitrate.—(History) Hildebrandt, Zt. angew. Ch., 39, 1926, 90; Nicol, Jl. Soc. Ch. Ind., 51, 1932, 971; von Lippmann, C.A., 22, 1928, 894; Mehring, Jl. Ind. Eng. Ch., 21, 1929, 379. (Sal Prunella) Anon., Jl. A.Ph.A., 18, 1929, 481. (Production) Anon., Ph. Jl., 12, 1852, 30; Hamid, Jl. Soc. Ch. Ind., 45, 1926, 315T; Mehring, Jl. Ind. Eng. Ch., 21, 1929, 379; Küpper, C.A., 25, 1931, 3441. (Nitrifying bacteria) Schloesing and Müntz, Comptes rend, 1879, through Warrington, Jl. Ch. Soc., 59, 1891, 495.

Gunpowder.—(History) Guttmann, Ch. Zt., 34, 1910, 794; Berger, Sch. Wsch. f. Ch. u. Ph., 50, 1912, 729; Anon., Ch. and Dr., 93, 1920, 1565; Davis, Jl. Ind. Eng. Ch., 20, 1928, 772, Robertson, Jl. Soc. Ch. Ind., 43, 1924, 801. (Explosion) Schwartz, Fire and Explosion Risks, p. 44; Darapsky, C.A., 1, 1907, 1059; Burlot, C.A., 19, 1925, 1776.

Potassium Permanganate.—(History) Anon., Jl. Soc. Ch. Ind., 42, 1923, 386; Cattelain, C.A., 24, 1930, 310. (Manufacture) Schütz, Zt. angew. Ch., 24, 1911, 1628. (Properties) Mooney, C.A., 25, 1931, 3892. (Oxidizing action) Jones, Jl. Ch. Soc., 33, 1878, 98; Fales and Roller, Jl. Am. Ch. Soc., 51, 1929, 345. (Uses) Rand, A.J.P., 42, 1870, 547. (Condy's fluid) Anon., A.Ph.A., 34, 1886, 250.

CHAPTER XXVI

SODIUM

Symbol, Na. Atomic weight, approximately 23

The symbol Na is an abbreviation of the word *natrium*, this being derived from natron, which was from the Greek word *nitron*, which was the original name of the carbonate. Our English word sodium is derived from soda, which comes from the word *sodash*, this hinting its preparation from the ashes of "sods," or marine plants.

Sodium, like potassium, was isolated by Sir Humphry Davy in 1807 by the electrolysis of the hydroxide. (See p. 459.)

Occurrence.—The most abundant source of sodium is common salt, or sodium chloride, this being a constituent of sea water, but chiefly obtained in commerce either from mines or by the evaporation of brine from salt wells. Sea water is a scarcely available source of sodium chloride, because therein are found chlorides of many other elements which are separated with difficulty.

Isolation.—The element sodium is isolated by a process quite similar to that by which we obtain potassium, viz., by heating carbonate with coal, chalk being added as a flux. This process is not so dangerous as is the preparation of potassium, inasmuch as the sodium carbonyl, NaCO, does not solidify in the delivery tube. (See p. 459.)

Metallic sodium is now being made by treating sodium hydroxide with iron carbide at a temperature of 1000° C.

It is also obtained by the electrolysis of sodium hydroxide in the same manner employed in isolating potassium.

Properties.—Sodium is a soft, silvery-white metal, lighter than water (sp. gr. 0.971) resembling potassium, and, like it, is so easily oxidized that it must be kept under petroleum. When metallic sodium and mercury are rubbed together, an amalgam results which, when brought into contact with moisture, ignites. This mixture has been used as a cigar-lighter, but its danger was such that it never became popular.

The characteristic tests of the element and its salts are the yellow color that it communicates to a colorless flame; a white precipitate formed when a solution of sodium salt is brought into contact with a solution of pyroantimoniate of potassium.

The sodium flame is counted among the most delicate of tests, it having been estimated that $\frac{1}{65,000,000}$ grain will respond thereto. By reason of its sensitiveness the positive testing of sodium with the flame is difficult, as almost anything tested will give a yellow flame by reason of the presence of minute traces of sodium. Hence the chemist trains his eye to a rough estimation of the quantity shown by the intensity for the flame, rather than by the bare fact of the presence of a yellow color.

The following compounds of sodium and their preparations are official:

Sodium hydroxide	90	per cent	absolute.	NaOH.
Sodium acetate	99	"	"	$NaC_2H_3O_2.3H_2O$.
Sodium benzoate	99	"	"	$NaC_7H_5O_2$.
Sodium bicarbonate	99	"	"	$NaHCO_3$.
Sodium biphosphate	98	"	"	NaH_2PO_4. (after drying)
Sodium borate	99	"	"	$Na_2B_4O_7.10H_2O$.
Sodium perborate	86.5	"	"	$NaBO_3.4H_2O$.
Sodium bromide	99	"	"	NaBr.
Monohydrated sodium carbonate	99.5	"	"	Na_2CO_3. (after drying)
Sodium chloride	99.5	"	"	NaCl.
Physiological solution of sodium chloride contains 8.5 Gm. sodium chloride to the liter.				
Sodium citrate	99	"	"	$Na_3C_6H_5O_7$. (after drying)
Sodium iodide	99	"	"	NaI.
Sodium nitrite	95	"	"	$NaNO_2$.
Sodium phosphate	99	"	"	Na_2HPO_4. (after drying)
Exsiccated sodium phosphate	98	"	"	Na_2HPO_4.
Effervescent sodium phosphate	20	per cent	exsiccated	sodium phosphate.
Sodium salicylate	99.5	"	absolute.	$NaC_7H_5O_3$.
Sodium sulfate	99	"	"	Na_2SO_4. (after drying)
Sodium thiosulfate	99	"	"	$Na_2S_2O_3$. (after drying)

We might also add:

Potassium and sodium tartrate (considered among the potassium salts).
Solution of chlorinated soda (considered among the chlorine preparations).
Surgical solution of chlorinated soda (considered among the chlorine preparations).
Sodium benzosulfinide, or soluble gluside, U.S.P. X (considered among the benzoic acid derivatives).
Sodium cacodylate (considered among the arseno-organics).
Sodium indigotindisulphonate (considered among the indigo derivatives).

SODII HYDROXIDUM—Sodium Hydroxide

(Sod. Hydrox.—Caustic Soda)

NaOH. Molecular weight, 40.00

Sodium Hydroxide contains not less than 95 per cent of total alkali, calculated as NaOH, of which not more than 3 per cent is Na_2CO_3.

Caution.—Great care is necessary in handling sodium hydroxide, as it rapidly destroys organic tissues.

Storage.—Preserve in air-tight containers. If bottles are used they must be of hard glass, and cork stoppers should be paraffined.

Summarized Description.

Dry, white flakes, fused masses, pellets, or brittle sticks; very caustic; deliquescent in air, absorbing both water and carbon dioxide; soluble in about 1 part of water and very soluble in alcohol. For details see U.S.P., p. 342.

For ***tests for identity***, for ***impurities*** (organic matter, insoluble impurities, potassium, heavy metals) and for ***assay*** see U.S.P., p. 342.

Remarks.—Soda is prepared by the evaporation of a solution of soda. It occurs in irregular lumps or in cylindric sticks, just as does potassa, and is, in fact, very similar to potassa, being decidedly caustic and possessing the same soapy taste, which is a distinguishing characteristic of the alkalis. It differs from potassa, however, in being less deliquescent. The terms "soda" and "potassa" are convenient words for sodium hydroxide and potassium hydroxide although they belong to an earlier age of chemical terminology.

Soda cum Calce (N.F. IV) is a mixture of equal quantities of sodium hydroxide and calcium oxide. It is sometimes called *London paste.*

Liquor Sodii Hydroxidi (U.S.P. X) or *solution of sodium hydroxide* is an aqueous solution, containing about 5 per cent of absolute NaOH. It is prepared by a process analogous to that of the manufacture of the solution of potassa, by treatment of sodium carbonate with calcium hydroxide, as shown in the following equation:

$$Na_2CO_3 + Ca(OH)_2 = 2NaOH + CaCO_3.$$

It is also a side product in the electrolytic production of chlorine (see p. 419).

Note that the words sodium and soda are not to be used indiscriminately. Sodium is an element, while soda is the hydroxide of that element. Note the absurdity and real danger of the term "soda water," which is a solution of carbonic oxide in water.

The solution of soda is used as an antacid.

Dose.—1 cc. (15 minims), very largely diluted.

Sodium Peroxide, Na_2O_2, has been mentioned on page 412 under the name, *oxone.* It is now manufactured on a large scale as a side-product in alkali manufacture and is used extensively as a bleaching agent.

LABORATORY EXERCISE

MAKE SOLUTION OF SODA, U.S.P., 1890

Recipe.—	Sodium carbonate	42.5 Gm.
	Lime	12.5 Gm.
	Distilled water, a sufficient quantity.	

Dissolve the sodium carbonate in 100 cc. of boiling distilled water. Slake the lime with about 7½ cc. of distilled water, then mix it well with 100 cc. of distilled water, pour the mixture into a tared flask, and, having heated it to boiling, gradually add to it the solution of sodium carbonate and boil during ten minutes. Then add enough distilled water to the flask to make the contents weigh 250 Gm., and set the flask aside, well stoppered, until the contents are cold. Lastly, strain the liquid through linen, set it aside in a well-stoppered bottle until it has become clear by subsidence, and separate the clear solution by decantation or by means of a syphon.

Explanation.—*Monohydrated sodium carbonate,* U.S.P. X, 18.4 Gm. may be used instead of the above amount of crystalline sodium carbonate. The chemical reaction in this process is as follows:

$$Ca(OH)_2 + Na_2CO_3 = NaOH + CaCO_3.$$

The result of the reaction is a liquid containing sodium hydroxide in solution, and a sediment consisting of calcium carbonate (precipitated chalk).

The equation given above is purposely left incomplete. Complete this so that the amount of each element on the two sides of the sign of equality is the same.

Again, the equation does not represent the truth as far as the constituents directed in the foregoing recipe are concerned. Lime is not calcium hydroxide, but is calcium oxide, the hydroxide being produced only after slaking the lime, the reaction being $CaO + H_2O = Ca(OH)_2$.

Again, the sodium carbonate directed above is not the exsiccated Na_2CO_3, but the crystalline salt containing 10 molecules of water of crystallization. So the real reaction runs:

$$CaO + H_2O + Na_2CO_3 10H_2O = NaOH + CaCO_3.$$

Be sure to complete this equation before proceeding further.

Calculations.—Figure out molecular weight of the five substances in above equation, viz.:

Ca atomic weight = ——	Ca = 1 $\times$ —— = ——
O atomic weight = ——	O = 1 $\times$ —— = ——
	CaO molecular weight = ——

H atomic weight = ——	H_2 = 2 $\times$ —— = ——
O atomic weight = ——	O = 1 $\times$ —— = ——
	H_2O molecular weight = ——

Na atomic weight = ——	Na_2 = 2 $\times$ —— = ——
C atomic weight = ——	C = 1 $\times$ —— = ——
O atomic weight = ——	O_3 = 3 $\times$ —— = ——
H_2O molecular weight = ——	$10H_2O$ = 10 $\times$ —— = ——
	$Na_2CO_310H_2O$ molecular weight = ——

Na atomic weight = ——	Na = 1 $\times$ —— = ——
O atomic weight = ——	O = 1 $\times$ —— = ——
H atomic weight = ——	H = 1 $\times$ —— = ——
	NaOH molecular weight = ——

NaOH molecular weight = ——. The actual weight of NaOH produced from above equation is this molecular weight *times* the number of molecules produced.

Ca atomic weight = ——	Ca = 1 $\times$ —— = ——
C atomic weight = ——	C = 1 $\times$ —— = ——
O atomic weight = ——	O_3 = 3 $\times$ —— = ——
	$CaCO_3$ molecular weight = ——

Now write the equation last given with the correct number of molecules, and place under each substance the figures expressing the molecular weights, or, in case more than a molecule of a substance is involved, the combining weights. Then reckon out the following problems:

1. How many grams absolute sodium hydroxide in 250 Gm. of 5 per cent solution of soda?

2. How many grams of lime (CaO) and of crystallized sodium carbonate ($Na_2CO_3 + 10H_2O$) needed to make 80 Gm. absolute soda (NaOH)?

3. How many grams of lime and of crystalline sodium carbonate needed to make 12.5 Gm. absolute soda?

If monohydrated sodium carbonate is used, the equation will run:

$$CaO + H_2O + Na_2CO_3H_2O = NaOH + CaCO_3.$$

(Complete this equation).

The molecular weight calculation, as far as the sodium carbonate is concerned will be:

Na atomic weight ——	Na_2 = 2 $\times$ —— = ——
C atomic weight ——	C = 1 $\times$ —— = ——
O atomic weight ——	O_3 = 3 $\times$ —— = ——
H_2O molecular weight ——	H_2O = 1 $\times$ —— = ——
	$Na_2CO_3H_2O$ molecular weight = ——

For table of atomic weights, see p. 390.

For complete figuring of molecular weights, see p. 400.

For details of balancing equations, see p. 448.

Remarks on Process.—*Dissolve the sodium carbonate* in pint flask, and when solution is complete, put into an 8-ounce wide-mouthed bottle. Filter only if necessary—if containing dirt.

Be sure that the sodium carbonate is not effloresced. For this reason the noneffflorescent monohydrated sodium carbonate is better.

Slake the lime by placing a lump in a mortar and adding the water, drop by drop, so it can be absorbed by the lime.

Better do this before dissolving the sodium carbonate, as with the small amount of lime used the slaking will take some time. Do not expect the generation of a large amount of heat in slaking the minute quantity of lime. Heat *is* developed, but in scarcely appreciable quantity. Slaking of the lime may be hastened by warming mortar on radiator.

When the lime is slaked, it will crumble to a powder. This takes, with the small amount of lime employed, fifteen minutes to a half hour. When lime is slaked, *mix* *it well with water.* That is, triturate with, say, 75 cc. of the water, making a milky paste (milk of lime); pour this into flask, and wash mortar and pestle with the other 25 cc. water, pouring washings into flask containing the milk of lime.

Be sure to tare flask before pouring in the milk of lime. The rest of the directions given above need no special remarks, except the statement that—

The *finished product is not to be filtered:* at least, through paper, as the alkali will eat the paper. Asbestos wool can be used, however; a bit of this being inserted into funnel as if it were a plug of cotton. The foregoing recipe, however, directs decantation.

The *precipitated chalk is to be thrown away,* as it cannot be freed from the alkali except by extraordinary effort.

SODII ACETAS—Sodium Acetate

(Sod. Acet.)

$NaC_2H_3O_2.3H_2O$. Molecular weight, 136.07

Sodium Acetate, when rendered anhydrous by drying at 120° C., contains not less than 99 per cent of $CH_3.COONa$. It contains not less than 36 per cent and not more than 41 per cent of water.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless, transparent, monoclinic prisms or granular powder; cooling saline taste; somewhat efflorescent; soluble in about 0.8 part of water and about 15 parts of alcohol. For details see U.S.P., p. 334.

For *tests for identity,* for *impurities* (potassium, alkali, arsenic, heavy metals) and for *assay* see U.S.P., p. 334.

Remarks.—Sodium acetate, like the potassium salt, is made from acetic acid, and the "stock" salt of the metal. It will be remembered that the stock salt of potassium—the one usually employed in the manufacture of ordinary salts of that metal—was the bicarbonate, the carbonate being inadmissible by reason of its indefinite quality. With sodium compounds the "stock" salt is the carbonate, as it is readily crystalline and quite stable if kept in a well-corked bottle. Its tendency is toward efflorescence—not deliquescence—such is the usual inclination of sodium compounds; just as soda soap—Castile soap—grows hard and dry on standing: while potassa soap—soft soap—and other potassium compounds are usually deliquescent.

Sodium acetate is made by the action of acetic acid on sodium carbonate, and the latter salt is used in the manufacture of most sodium compounds. Let us compile a list of official sodium salts prepared from the carbonate:

Sodium benzoate from benzoic acid and sodium carbonate.
Sodium bromide from ferrous bromide and sodium carbonate.
Sodium iodide from ferrous iodide and sodium carbonate.
Sodium phosphate from acid calcium phosphate and sodium carbonate.
Sodium salicylate from salicylic acid and sodium carbonate.

The pharmaceutic value of sodium carbonate can thus be seen.

Sodium acetate occurs in the form of colorless, transparent crystals, or in a granular powder, and must be kept in well-stoppered bottles since it is efflorescent in warm, dry air and is therefore likely to lose its water of hydration.

Dose.—1.5 Gm. (25 grains).

SODII BENZOAS—Sodium Benzoate

(Sod. Benz.)

Sodium Benzoate, when dried to constant weight at 110° C., contains not less than 99 per cent of C_6H_5COONa.

Storage.—Preserve in well-closed containers.

Summarized Description.

White, amorphous, granular or crystalline powder; sweetish taste; soluble in about 1.8 parts of water and about 49 parts of alcohol. For details see U.S.P., p. 335.

For *tests for identity*, for *impurities* (alkali, heavy metals) and for *assay* see U.S.P., p. 335.

Remarks.—This salt, the manufacture of which is outlined on the preceding page has been subject to considerable controversy during the past thirty years because of its use as a food preservative.

Dose.—1 Gm. (15 grains).

SODII BORAS—Sodium Borate

(Sod. Bor.—Borax, Sodium Tetraborate)

$Na_2B_4O_7.10H_2O$. Molecular weight, 381.43

Sodium Borate contains not less than 52.32 per cent and not more than 54.92 per cent of $Na_2B_4O_7$, corresponding to not less than 99 per cent of $Na_2B_4O_7.10H_2O$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless, monoclinic prisms or white powder; sweetish alkaline taste; slightly efflorescent; soluble in about 16 parts of water and in 1.25 parts of glycerin; insoluble in alcohol; on heating it melts, then forms a porous mass and then fuses to a glassy mass. For details see U.S.P., p. 337.

For *tests for identity*, for *impurities* (carbonates, bicarbonates, heavy metals, arsenic) and for *assay* see U.S.P., p. 337.

Sodium borate—ordinary *borax*—is a valuable and interesting chemical. Its formula, $Na_2B_4O_7$, seems difficult, and appears contradictory to the formula of boric acid already given—H_3BO_3—but investigation clears up the matter. Remember that the valence of boron is III; that boric acid is a true ortho-acid—$B(OH)_3$ or H_3BO_3. True sodium borate has the formula Na_3BO_3, and what we call sodium borate is not the true salt but a "*pyroborate.*" The Greek word for fire is "*pyros,*" and all chemicals bearing the prefix "*pyro*" are bodies formed under influence of high heat. In passing, such examples as "pyroligneous acid" (crude acetic acid), "pyrogallic acid," and "pyrophosphoric acid" may be cited. Like these, pyroboric acid and pyroborates are made by subjecting the other substance to heat.

Let us see what will occur when boric acid is heated. It will, of course, like all ortho-acids, lose water, and, under proper conditions, in a most peculiar ratio:

Taking $4H_3BO_3$, this carried out gives . .	$H_{12}B_4O_{12}$
Let us subtract from this $5H_2O$	$H_{10}\ O_5$
We then have left pyroboric acid	$H_2\ B_4O_7$

the sodium salt of which, $Na_2B_4O_7$, is official borax, which is a natural product, being found in certain lakes throughout the world. The impure borax, obtained by spontaneous evaporation of the waters of these lakes, is called *tincal.* At the present time practically all the American borax is obtained from the borax lakes found in the Death Valley of Nevada. It is also made by treating the native boric acid of Tuscany with sodium carbonate.

Borax occurs either in colorless, transparent prisms or in a white powder, odorless, and having a sweetish, alkaline taste.

It is soluble in 16 parts of water and in 1¼ parts of glycerin. When heated, it fuses and solidifies into a transparent solid called borax glass. This borax glass is used quite largely in analytic work under the name of borax bead, the chemical being fused on loop of platinum wire, thereby forming a minute globule of borax glass. When this body is melted with certain metallic salts, the body is given characteristic colors. (See p. 997.)

Borax is one of the most valuable of the sodium compounds. It is used in numerous operations where a mild alkali is indicated, completely possessing the character of an alkali, and yet acts in a manner much milder than does either sodium carbonate or the bicarbonate. This explains its extensive use in cleaning delicate fabrics, such as fine cloth or hair, where stronger alkalis would act disastrously. It is also a valuable antiseptic, and for such purposes it is (improperly) used as a preservative for meats and food. In medicine it is used as a mild antiseptic, chiefly externally.

Compound Solution of Sodium Borate (N.F.), or *Dobell's Solution*, is rather largely used as a nasal douche. (See p. 214.) It is made by dissolving sodium borate and bicarbonate in water followed by the addition of glycerin and liquefied phenol. The vigorous effervescence which results is due to the liberation of boric acid by action of the glycerin and the reaction between the acid and the bicarbonate.

SODII PERBORAS—Sodium Perborate

(Sod. Perbor.)

$NaBO_3.4H_2O$. Molecular weight, 153.88

Sodium Perborate contains not less than 9 per cent of available oxygen, corresponding to about 86.5 per cent of $NaBO_3.4H_2O$.

Storage.—Preserve in well-closed containers, in a cool place.

Summarized Description.

White crystalline granules or powder; odorless; saline taste; stable in dry air but liberates oxygen in moist air; soluble in water, solution decomposing into sodium metaborate and hydrogen peroxide. For details see U.S.P., p. 344.

For *tests for identity*, for *impurities* (heavy metals) and for *assay*, see U.S.P., p. 344.

Remarks.—Sodium perborate, $NaBO_3$, is made by treating borax with sodium hydroxide and sodium dioxide. It is also made by passing a current of electricity through a solution of borax, sodium bicarbonate, and a small amount of potassium dichromate.

Sodium perborate is a white powder sparingly soluble in water, but forming a stable solution having the action of hydrogen dioxide. When treated with diluted sulfuric acid, hydrogen dioxide is evolved. It is now in considerable demand as a nonirritating antiseptic and is used in dusting powders and mouth washes where the effect of a dioxide is desired.

Dose.—0.06 Gm. (1 grain).

Sodii Perboras Aromaticus (N.F.) or *N.F. Aromatic Sodium Perborate* represents the perborate flavored and sweetened with 4 per cent of oil of peppermint and 4 per cent of soluble saccharin. For further details see N.F. VI, p. 330. This is a new official, presenting a standard recipe for the very popular perborate dentifrices.

SODII BROMIDUM—Sodium Bromide

(Sod. Bromid.) M

NaBr. Molecular weight, 102.91

Sodium Bromide, when dried to constant weight at 100° C., contains not less than 99 per cent of NaBr.

Storage.—Preserve in air-tight containers.

Summarized Description.

Colorless cubical crystals or white granular powder; saline taste; somewhat hygroscopic; soluble in about 1.1 parts of water and in about 13 parts of alcohol. For details see U.S.P., p. 337.

For *tests for identity*, for *impurities* (alkali, iodides, heavy metals, bromates, sulfates, barium, and arsenic) and for *assay* see U.S.P., p. 338.

Remarks.—This chemical is made by methods analogous to those employed in making potassium bromide; that is, by treatment of sodium hydroxide with bromine, and the subsequent heating of the mixture with charcoal, or by the double decomposition of ferrous bromide with sodium bicarbonate.

Sodium bromide occurs in white, cubic crystals which are soluble in 1.1 parts of water. While potassium bromide dissolving in water produces a chilled liquid, sodium bromide and water make a warm solution. Hemm claims that this is due to the hydration of sodium bromide in dissolving. The crystals attract moisture, but do not liquefy therein. It is used as a mild sedative, closely resembling potassium bromide in action.

Dose.—1 Gm. (15 grains).

SODII CARBONAS MONOHYDRATUS—Monohydrated Sodium Carbonate

(Sod. Carb. Monohyd.)

$Na_2CO_3.H_2O$. Molecular weight, 124.01

Monohydrated Sodium Carbonate, when rendered anhydrous by gentle ignition, contains not less than 99.5 per cent of Na_2CO_3 and not less than 10 per cent and not more than 15 per cent of water.

Storage.—Preserve in well-closed containers.

Summarized Description.

White crystalline powder; strongly alkaline; efflorescent in dry air or at 50° C.; soluble in about 3 parts of water and in 8 parts of glycerin; insoluble in alcohol. For details see U.S.P., p. 339.

For *tests for identity*, for *impurities* (heavy metals) and for *assay* see U.S.P., p. 339.

Remarks.—Sodium carbonate, the next chemical demanding our attention, is, with the exception of sulfuric acid, the most widely used manufactured product in the chemical world. To mention all the many important industries in which sodium carbonate is a potent factor would occupy too much space, but chief among the branches of trade to which sodium carbonate is essential are soap-making and glass manufacture.

In ancient days the only source of sodium carbonate was by evaporation of water from certain soda lakes, such as *trona* from Egypt, or from the crude salt obtained by lixiviating the ashes of seaweeds, rich in soda, such as *barilla* from Spain. The output from these sources was rather limited, and as the soap and glass industries became more important the need for cheap sodium carbonate became more and more imperative, and, accordingly, a prize was offered by the Paris Academy, in 1782, for the best method of artificial production of this valuable alkali, and the prize was awarded to Nicholas Leblanc. In 1794 the French government took charge of his factory.

A most striking proof of the value of the process is shown by the fact that to this day a large amount of sodium carbonate is still manufactured by the Leblanc process.

In passing, it should be mentioned that Leblanc's process, like most other great discoveries, did not originate solely with the man whose name it bears. Duhamel in 1736 converted sodium chloride successfully into sodium sulfate, sodium sulfide, sodium acetate, and lastly into sodium carbonate. Marggraf, 1759, shortened the transformation by converting sodium chloride into sodium sulfate, then into sodium nitrate, and this, by strong heat, into the oxide which, on standing, absorbed enough carbon dioxide from the air to change into carbonate.

It is even said that the last portion of the Leblanc process (use of coal and limestone) was suggested to him by De la Mitherie, but be this as it may, it was Leblanc who established the first factory for the manufacture of sodium carbonate, and to him the real credit is due.

Leblanc chose as the sodium compound on which to begin operations that which was most widely distributed; that body which was found both on land and in the sea—sodium chloride or common salt. This is the cheapest sodium compound, and the only reason it is not used as the "stock salt" in chemical manufacturing—in making other sodium salts—is because of the difficulty with which it decomposes, there being very few acids which can break it up. Among these is sulfuric acid, the reaction being $2NaCl + H_2SO_4 = Na_2SO_4 + 2HCl$. Note that hydrochloric acid, HCl, is a side-product in the process. In England, when the manufacture was first begun, the acid was allowed to escape with the air through tall chimneys, with serious results—as the vapor mingled with the aqueous vapor and fell with the latter as rain, destroying vegetation and ruining health. So great was the damage that stringent laws were enacted prohibiting the discharge of the acid vapor. Thereupon the manufacturers took to condensing the vapors and disposing of the hydrochloric acid, and by curious change of times, at present, the keen competition has so lessened the price of sodium carbonate that the manufacturers gain much of their profit from the sale of the acid.

But to return to the process, which we have only followed to the formation of sodium sulfate, and which seems as far off as was the chloride, Leblanc's genius solved the problem of conversion. He realized that while the sulf*ate* was a very stable body, the sulf*ide* was quite weak—could be replaced even by the CO_3 group.

The changing of the sulfate, Na_2SO_4, to the sulfide, Na_2S, is very simple. It is merely a process of reduction, and is performed by the reducing agent we used in the manufacture of sulfurous acid—the element carbon, usually in the form of common coal. The reaction is as follows:

$$Na_2SO_4 + C_2 = 2CO_2 + Na_2S.$$

Having converted the strong sulfate into the easily dissociated sulfide, the next step is to bring about a double decomposition between this sulfide and some cheap carbonate. The carbonate best answering this requirement is the calcium salt, which is abundantly found as marble, limestone, chalk, and oyster shells. This salt is accordingly employed, and the reaction is:

$$Na_2S + CaCO_3 = Na_2CO_3 + CaS.$$

In practice, the sulfate is heated with coal and limestone at the same time, hence the two reactions run simultaneously.

The next process we have to consider is that which leads to the sodium bicarbonate instead of to the carbonate. This is the *Solvay process*, and is one of the most clear-cut processes we meet in chemistry, as both reaction products are valuable, and there is little waste-product. It is also called the "ammonia soda process," after the constituents employed.

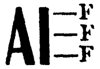
Like Leblanc's process, it starts off with that most abundant source of sodium, the chloride.

A solution of salt is placed in a tin-lined vat and is saturated with ammonia gas. This liquid, on cooling, is pumped into a second vat, where it absorbs carbon dioxide gas and forms sodium bicarbonate and ammonium chloride by the following reaction:

$$NaCl + NH_3 + H_2O + CO_2 = NaHCO_3 + NH_4Cl.$$

The process while comparatively modern has now outstripped the Leblanc process as far as total production is concerned as it is less wasteful and yields a finer and more attractive product.

The third method for obtaining the carbonic acid compounds of sodium is by the *cryolite process*, which is named from the Greenland mineral, which is the stock salt. Cryolite is a fluoride of aluminum and sodium, the formula of which is not so difficult if one only remembers that fluorine forms compounds entirely analogous to the chlorides, the bromides, and the iodides. Aluminum fluoride is AlF_3, since aluminum is trivalent and the linkage is graphically as follows:



$$\mathrm{Al}\begin{array}{l}-\mathrm{F}\\-\mathrm{F}\\-\mathrm{F}\end{array}$$

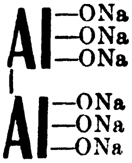
When written double, the formula is Al_2F_6. Sodium fluoride is NaF—exactly analogous to NaCl. The proportions in which these two fluorides combine are 6 molecules of NaF to one of Al_2F_6.

The method of manufacture of the sodium from cryolite has not the extended use that Leblanc's and Solvay's processes enjoy, it being practically a monopoly of one corporation.

Cryolite is first heated with limestone, and is thus converted into sodium aluminate and calcium fluoride, as shown in the following equation.

$$Al_2F_66NaF + 6CaCO_3 = Al_2(ONa)_6 + 6CaF_2 + 6CO_2.$$

The graphic formula of sodium aluminate is supposed to be as follows:



$$\begin{array}{l}\mathrm{Al}\begin{array}{l}-\mathrm{ONa}\\-\mathrm{ONa}\\-\mathrm{ONa}\end{array}\\ \,|\\ \mathrm{Al}\begin{array}{l}-\mathrm{ONa}\\-\mathrm{ONa}\\-\mathrm{ONa}\end{array}\end{array}$$

That is, aluminum hydroxide (p. 548) with its 6 atoms of hydrogen replaced by 6 atoms of sodium.

It is met with in analytic chemistry, one of the tests for aluminum being that any soluble salt of this metal, when treated with sodium hydroxide, yields a gelatinous precipitate, aluminum hydroxide, which is soluble in an excess of sodium hydroxide (p. 548).

This view is combated by physical chemists who reason that if this be true aluminum hydroxide should liberate hydrogen ions. They therefore deny the existence of sodium aluminate stating that the phenomenon is due to the "peptizing" (see p. 408) of $Al(OH)_3$ by sodium hydroxide.

Some investigators now claim that its formula is $Al\ (OH)_2ONa$, while others claim it is not a true salt but a colloidal condition.

In other words, when an excess of sodium hydroxide is added, the aluminum hydroxide combines with it to form a soluble aluminate of sodium, just described. This reaction is also employed in the separation of iron from aluminum in analytic work.

Returning to our cryolite process: the aluminate of sodium is converted into sodium carbonate by treatment with carbon dioxide gas by the following reaction:

$$Al_2(ONa)_6 + 3CO_2 = 3Na_2CO_3 + Al_2O_3.$$

The commercial value of this method of manufacturing sodium carbonate is due not only to the output of sodium carbonate, but also to the fact that the side-products—aluminum oxide and calcium fluoride—are worked up into the alums and the fluorine derivatives respectively.

Mention should be made of the fact that native sodium carbonate is now being purified and marketed at Searles Lake, California and also in Kenya and South Africa.

Sodium carbonate is an antacid, but is not used much internally, the less irritating bicarbonate being preferred.

Dose.—250 mg. (4 grains).

Sodii Carbonas (U.S.P. 1890) was the crystalline dekahydrated form, that is, containing 10 molecules of water of crystallization—$Na_2CO_3 10H_2O$. This is what is familiarly called *washing soda*, and had the disadvantage of being very efflorescent; so much so that the writer has seen crystals of the salt lose water while still in the crystallizing vat. This made it a matter of difficulty to employ the salt in work involving molecular proportions; hence in the eighth revision the monohydrated salt was given official recognition. Because the monohydrated salt is both stable and concentrated, it replaced both the crystalline and the exsiccated carbonate of the old Pharmacopœia.

Sodii Carbonas Exsiccatus (U.S.P. 1890).—This substance is made by taking dekahydrated sodium carbonate and exsiccating it at a temperature of about 45° C. (115° F.) until the product has lost half its weight. The object of using the heat of a water bath is in order to avoid the possible loss of carbon dioxide. The dry carbonate is used for the same purpose as in the dekahydrated, but is about twice the strength, and is preferable for filling prescriptions of pills and powders.

SODII BICARBONAS—Sodium Bicarbonate

(Sod. Bicarb.—Baking Soda)

$NaHCO_3$. Molecular weight, 84.00

Sodium Bicarbonate, when dried to constant weight over sulfuric acid, contains not less than 99 per cent of $NaHCO_3$.

Storage.—Preserve in well-closed containers, in a cool place.

Summarized Description.

White, crystalline powder; cooling, mildly alkaline taste; soluble in about 10 parts of water; insoluble in alcohol; aqueous solution loses carbon dioxide on boiling, being converted into the normal carbonate. For details see U.S.P., p. 335.

For *tests for identity*, for *impurities* (ammonia, carbonate, heavy metals, and arsenic), and for *assay* see U.S.P., p. 335.

Remarks.—While the commonly accepted formula for sodium bicarbonate is $NaHCO_3$, that is, H_2CO_3 with 1 atom of hydrogen replaced by 1 atom of sodium, Bicher claims for it the double formula $Na_2H_2(CO_3)_2$ and expresses this by means of an ingenious graphic formula.

The process for making this salt is by treating sodium carbonate with carbon dioxide. The Solvay process just described produces a crude bicarbonate but this is contaminated with ammonia and is calcined into carbonate and is then crystallized.

Sodium bicarbonate usually occurs in the form of a white, opaque powder, which is soluble in 10 parts of water; therefore much less soluble than is the carbonate. Sodium bicarbonate, not only effervesces with practically all acids, but also liberates CO_2 when treated with a number of chemicals such as bismuth subnitrate and even with borax when glycerin is the solvent. This fact is important in prescription compounding. Sodium bicarbonate is a popular antacid, being comparatively free from irritating action.

Dose.—1 Gm. (15 grains).

SODII CHLORIDUM—Sodium Chloride

(Sod. Chlorid.)

NaCl. Molecular weight, 58.45

Sodium Chloride, when dried to constant weight at 110° C., contains not less than 99.5 per cent of NaCl.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless cubical crystals or white, crystalline powder; purely saline taste; slightly hygroscopic; soluble in 2.8 parts of water; slightly soluble in alcohol; on heating, it decrepitates, fuses at 803° C. and finally volatilizes. For details see U.S.P., p. 340.

For *tests for identity,* for *impurities* (calcium, magnesium, barium, bromide, iodide), and for *assay* see U.S.P., p. 340.

Sodium chloride, or *common salt,* is one of the most valuable and ancient of the chemicals. It is essential to animal economy, hence it has been used from the earliest days. As mentioned above, it is the chief source of metallic sodium and of the sodium compounds, and is found in the native state widely distributed.

Its presence in sea water, salt wells, and salt mines has been mentioned, so here it is only necessary to state that, among the chief deposits of salt, are the mines near Cracow, in eastern Poland; near Salzburg, in Tyrol; and the Petit Anse mines of southwest Louisiana. In many parts of the world are found deposits of salt of not sufficient area to justify mining. In these cases shafts are sunk until the deposit is reached, water poured in, and when saturated with the salt, is pumped out and the solution evaporated. Such process has been carried on in Cleveland, O. Another source of salt is the natural salt springs found in certain sections of the world. There are many of these in Germany of insufficient concentration to justify the use of heat for complete evaporation and in such cases the major portion of the water is removed by the application of spontaneous evaporation, explained on p. 106.

Liquor Sodii Chloridi Physiologicus (U.S.P.) or *Normal Saline Solution* is an $^{85}/_{100}$ of 1 per cent solution of sodium chloride that has been carefully sterilized. It is presumably of the same saline strength as blood serum, and is used for transfusion operations. For details see p. 211.

SODII CITRAS—Sodium Citrate
(Sod. Cit.)

$Na_3C_6H_5O_7.2H_2O$. Molecular weight, 294.06

Sodium Citrate, when rendered anhydrous by drying at 150° C., contains not less than 99 per cent of $C_3H_4.OH.(COONa)_3$. It contains not less than 10 per cent and not more than 13 per cent of water.

Storage.—Preserve in well-closed containers.

Summarized Description.

White, crystalline powder; cooling saline taste; soluble in 1.3 parts of water; insoluble in alcohol; carbonizes at red heat, leaving a residue of carbonate. For details see U.S.P., p. 341.

For *tests for identity,* for *impurities* (tartrate, arsenic, heavy metals, and lead) and for *assay* see U.S.P., p. 341.

Remarks.—This official is made by treating sodium carbonate with citric acid. It, like the other alkaline citrates, has the property of holding in solution such insoluble bodies as ferric phosphate and magnesium carbonate. It is used as a refrigerant.

Dose.—1 Gm. (15 grains).

SODII IODIDUM—Sodium Iodide
(Sod. Iodid.)

NaI. Molecular weight, 149.92

Sodium Iodide, when dried to constant weight at 120° C., contains not less than 99 per cent of NaI. It contains not more than 5 per cent of water.

Storage.—Preserve in air-tight containers.

Summarized Description.

Colorless, cubical crystals or white, crystalline powder; saline taste; deliquescent in moist air, turning brown; soluble in about 0.5 part of water, in about 1.6 parts of alcohol and in 1.25 parts of glycerin. For details see U.S.P., p. 342.

For *tests of identity*, for *impurities* (alkali, potassium, heavy metals, iodate, cyanide, nitrates, nitrites, thiosulfate) and for *assay* see U.S.P., p. 343.

Remarks.—This salt so closely resembles potassium iodide that little further information is needed here. It is made by the same processes used in the manufacture of potassium iodide and the bromides of potassium and sodium. Hence here it is only necessary to mention that treating sodium hydroxide with iodine, and subsequent heating of the evaporated mass with charcoal, will yield the iodide.

It occurs in anhydrous cubes or rhombic prisms, somewhat deliquescent, turning reddish brown on exposure to air, the latter change being due to liberation of iodine. It is used medicinally exactly as in potassium iodide and has recently been found of great value in the treatment of goiter.

Dose.—300 mg. (5 grains).

SODII NITRIS—Sodium Nitrite

(Sod. Nitris)

$NaNO_2$. Molecular weight, 69.01

Sodium Nitrite, when dried to constant weight over sulfuric acid, contains not less than 95 per cent of $NaNO_2$.

Storage.—Preserve in air-tight containers.

Summarized Description.

White, opaque, fused masses or sticks, colorless hexagonal crystals or granular powder; mild saline taste; deliquescent on exposure to air and oxidizes to nitrate; soluble in 1.5 parts of water; slightly soluble in alcohol; on heating at 270° C. melts and then dissociates into oxygen, nitrogen, nitrogen dioxide, and sodium oxide. For details see U.S.P., p. 343.

For *tests for identity*, for *impurities* (heavy metals) and for *assay* see U.S.P., p. 344.

Remarks.—This salt is made by reduction of sodium nitrate by fusing with sheet lead. The fused mass is poured into water, the diluted solution treated with nitric acid until just neutral (thus precipitating the lead). The filtrate is then concentrated, when the sodium nitrite crystallizes out.

This salt occurs in the form of deliquescent granules, or usually in the form of fused pencils. It was introduced in the Pharmacopœia in 1890, because used in the manufacture of spirit of nitrous ether, and has been retained in the present Pharmacopœia because of its marked hypotensive action, making it as useful, therapeutically, as nitroglycerin.

Dose.—60 mg. (1 grain).

Luff and Finnemore report that sodium nitrite reacts with ammonium bromide with explosive violence.

SODII PHOSPHAS—Sodium Phosphate

(Sod. Phos.)

$Na_2HPO_4.7H_2O$. Molecular weight, 268.13

Sodium Phosphate, when dried to constant weight at 110° C., contains not less than 98 per cent of Na_2HPO_4. It contains not less than 43 per cent and not more than 50 per cent of water.

Storage.—Preserve in air-tight containers.

Summarized Description.

Colorless, monoclinic prisms or granular salt; cooling saline taste; efflorescent; soluble in about 4 parts of water; insoluble in alcohol; on heating, is converted into sodium pyrophosphate. For details see U.S.P., p. 345.

For *tests for identity*, and for *impurities* (calcium, aluminum, heavy metals, carbonate, sulfate, chloride, arsenic) and for *assay*, see U.S.P., p. 345.

Remarks.—The formula of sodium phosphate is worthy of special notice. On p. 396 will be found the graphic formula of phosphoric acid, H_3PO_4. If two of the three hydrogen atoms of phosphoric acid are replaced by sodium atoms (each atom of sodium of valence I replacing 1 atom of hydrogen), we get Na_2HP_4O, the formula of the official sodium phosphate which is not to be confused with the *acid phosphate*.

All three hydrogen atoms found in phosphoric acid are replaceable under proper conditions as illustrated in the formula of official calcium phosphate $Ca_3(PO_4)_2$ (p. 397), and a sodium phosphate having the formula Na_3PO_4 can be made. (See p. 496.) Until recently Na_2HPO_4 was the only commercially available sodium phosphate. Of late years however the monosodium phosphate, NaH_2PO_4, has been used in medicine and found of such value that it is recognized in the present Pharmacopœia under the name, *sodium biphosphate* or *acid phosphate* (see p. 491).

Sodium phosphate, Na_2HPO_4, is prepared by treating bone ash with sulfuric acid, when acid calcium phosphate is produced, as shown in the following equation:

$$Ca_3(PO_4)_2 + 2H_2SO_4 = CaH_4(PO_4)_2 + 2CaSO_4.$$

The solution of acid calcium phosphate, freed from the insoluble calcium sulphate by forcible straining, treated with sodium carbonate, yields sodium phosphate, as shown in the following equation:

$$CaH_4(PO_4)_2 + Na_2CO_3 = Na_2HPO_4 + CaHPO_4 + CO_2 + H_2O.$$

Other authorities say the reaction runs:

$$3CaH_4(PO_4)_2 + 4Na_2CO_3 + 4Na_2HPO_4 + Ca_3(PO_4)_2 + 4H_2O + 4CO_2.$$

Sodium phosphate occurs in the form of large, colorless, efflorescent crystals, although now usually dispensed in the form of granules. It is important for the pharmacist to remember that these granules are efflorescent, that they part comparatively easily with a portion of their water of crystallization, and thus lose a considerable amount of their weight. In fact, in the writer's experience, he has known of cases where a pound of sodium phosphate decreased to 12 ounces by weight by simple efflorescence. In selling the salt this should be kept in mind, otherwise a depreciation in the profit will result.

Recent literature has shown that a large amount of sodium phosphate on the market is contaminated with arsenic, and therefore the pharmacist should examine his phosphate in order to prevent dispensing a dangerous chemical.

An interesting preparation of the salt is a combination of it with sodium nitrate and citric acid. When these three chemicals are triturated together in a warm mortar, they liquefy, forming a solution containing over 100 per cent by volume of sodium phosphate. A similar preparation is *compound solution of sodium phosphate* N.F. (p. 214).

Medical Properties.—A valuable saline purgative.

Dose.—4 Gm. (1 drachm).

SODII PHOSPHAS EFFERVESCENS—Effervescent Sodium Phosphate

For details of manufacture see below.

Remarks.—This is a granular effervescent salt containing 20 per cent exsiccated sodium phosphate. Note that the Pharmacopœia directs that the mass be softened for granulation by warming. It is a useful and agreeable purgative.

Dose.—10 Gm. (2½ drachms).

LABORATORY EXERCISE

MAKE EFFERVESCENT SODIUM PHOSPHATE

Exsiccated sodium phosphate	5.0 Gm.
Sodium bicarbonate	11.9 Gm.
Tartaric acid, dried and powdered	6.3 Gm.
Citric acid, in uneffloresced crystals	4.1 Gm.

Powder the citric acid and mix it intimately with the exsiccated sodium phosphate, add tartaric acid, then thoroughly incorporate the sodium bicarbonate.

Place the mixed powders on a plate of glass or in a suitable dish, in an oven heated to between 93° and 104° C.

When the mixture has acquired a moist consistence, by the aid of careful manipulation with a wooden spatula, rub it through a No. 6 tinned-iron sieve, and dry the granules at a temperature not exceeding 54° C. Keep the product in well-stoppered bottles.

Chemical Explanation.—In the recipe just given the exsiccated sodium phosphate is mixed with sodium bicarbonate, tartaric and citric acids and the mixture is then warmed until it becomes doughy, when it is granulated by rubbing through a coarse sieve. Heat produces a doughy mass because of the presence of water of crystallization in the citric acid, $H_3C_6H_5O_7 + H_2O$, the amount being sufficient to soften the mixture without very serious loss of carbon dioxide.

The dry granules contain, beside sodium phosphate, particles of sodium bicarbonate, tartaric acid and citric acid, and perhaps a small amount of the sodium salt of the two acids just mentioned. It is designed, however, to have the two acids and the bicarbonate rest side by side in uncombined form. As soon as the dried granules are thrown into water the three chemicals combine with violent effervescence (liberation of carbon dioxide) as shown in the following equations:

Sodium bicarbonate	plus	Citric acid	give	Sodium citrate	plus	Carbon dioxide	plus	water
$NaHCO_3$	+	$H_3C_6H_5O_7$	=		+		+	
Sodium bicarbonate	plus	Tartaric acid	give	Sodium tartrate	plus	Carbon dioxide	plus	water
$NaHCO_3$	+	$H_2C_4H_4O_6$	=		+		+	

Complete these equations.

Remarks on Process.—The recipe just given is similar to but not identical with that given in the present edition of the Pharmacopœia. The two recipes should be carefully compared by the student.

Thoroughly mix the four chemicals, sodium phosphate and bicarbonate, tartaric and citric acids, by trituration in a mortar.

The sodium phosphate must be exsiccated, since the crystalline salt contains 60 per cent of water, which would cause undue effervescence of the mass during mixing and granulating. Dried tartaric acid must likewise be used.

Soften the mixed powders by warming in an oven between 93° and 104° C. as mentioned above, the water of crystallization in the citric acid is just sufficient to cause an interaction between the chemicals with a reduction of the softening point of the mixture and the formation of a pasty mass which permits of granulation.

Push moist mass through clean coarse sieve, letting granules fall on paper placed beneath.

Dry granules by placing paper on radiator and put into dry bottle without great delay.

SODII PHOSPHAS EXSICCATUS—Exsiccated Sodium Phosphate

(Sod. Phos. Exsic.—Dried Sodium Phosphate)

Exsiccated Sodium Phosphate, when dried to constant weight at 110° C., contains not less than 98 per cent of Na_2HPO_4.

Storage.—Preserve in air-tight containers.

Condensed Recipe.

Allow crystals of sodium phosphate to effloresce at 25° to 30° C. for several days, then heat in an oven to 110° C. until the salt ceases to lose weight. Then powder and sift. For details see U.S.P. X.

Summarized Description.

White powder; soluble in about 8 parts of water; insoluble in alcohol. For details see U.S.P., p. 346.

For *tests for identity* and for *impurities*, see sodium phosphate. For *assay* see U.S.P., p. 346.

Remarks.—This is used for the manufacture of the granular effervescent salt just described. Note that its dose is just half of that of the crystalline salt.

Dose.—2 Gm. (30 grains).

SODII BIPHOSPHAS—Sodium Biphosphate

(Sod. Biphos.—Sodium Dihydrogen Phosphate, Monosodium Orthophosphate, Sodium Acid Phosphate)

$NaH_2PO_4.H_2O$. Molecular weight, 138.05

Sodium Biphosphate, when dried to constant weight at 100° C., contains not less than 98 per cent of NaH_2PO_4. It contains not less than 10 per cent and not more than 15 per cent of water.

Storage.—Preserve in air-tight containers.

Summarized Description.

Colorless crystals or white powder; freely soluble in water; insoluble in alcohol. For details see U.S.P., p. 336.

For *tests for identity* and for *impurities* (free acid, disodium phosphate, aluminum, calcium, sulfate, chloride, heavy metals, arsenic) and for *assay* see U.S.P., p. 336.

Remarks.—This official has been largely used in recent years for converting urine from an alkaline to an acid reaction especially when administering methenamine (p. 766). This latter chemical acts as an antiseptic only in acid urine and when the patient's urine is alkaline, sodium biphosphate is administered to render the urine acid. While ordinary sodium phosphate, Na_2HPO_4, is alkaline in reaction, sodium biphosphate has an acid reaction.

Dose.—600 mg. (10 grains).

SODII SALICYLAS—Sodium Salicylate

(Sod. Salicyl.)

$NaC_7H_5O_3$. Molecular weight, 160.04

Sodium Salicylate, when dried to constant weight at 100° C., contains not less than 99.5 per cent of $C_6H_4.OH.COONa$.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

White, micro-crystalline powder; scales or amorphous powder; colorless to faint pink; sweet saline taste; soluble in about 0.9 part of water and in about 7.5 parts of alcohol; on heating, it chars leaving residue of sodium carbonate. For details see U.S.P., p. 347.

For *tests for identity*, for *impurities* (sulfites, thiosulfates, heavy metals) and for *assay* see U.S.P., p. 347.

Remarks.—This salt is prepared by treating salicylic acid with sodium carbonate, and evaporating the resulting solution of sodium salicylate to dryness in the water bath. Many modern therapeutists claim that the salicylic acid employed should be that from oil of wintergreen. Calls for "Sodium salicylate (natural)" can be easily filled by the retail pharmacist by treating oil of wintergreen, or oil of sweet birch, with the molecular quantity of sodium hydroxide, evaporating the mass to dryness, redissolving in water, making the solution acid by the addition of more salicylic acid, and finally granulating the resulting filtered liquid. The addition of extra acid is essential, for the alkaline sodium salicylate is invariably of grayish color. In preparing the sodium salicylate great care must be taken to avoid contact with iron, as that element will color the salicylate a blood red. (See p. 800.)

Sodium salicylate is a valuable remedy for rheumatism.

Dose.—1 Gm. (15 grains).

SODII SULFAS—Sodium Sulfate

(Sod. Sulf.—Glauber's Salt)

$Na_2SO_4.10H_2O$. Molecular weight, 322.21

Sodium Sulfate, when rendered anhydrous by drying at 120° C., contains not less than 99 per cent of Na_2SO_4. It contains not less than 51 per cent and not more than 57 per cent of water.

Storage.—Preserve in well-closed containers.

Summarized Description.

Large, colorless, efflorescent, monoclinic prisms or granular crystals; bitter saline taste: soluble in about 1 part of water at 25° C. (see below); insoluble in alcohol; fuses in its water of crystallization at 33° C. For details see U.S.P., p. 348.

For *tests for identity*, for *impurities* (heavy metals, arsenic) and for *assay* see U.S.P., p. 348.

Sodium sulfate is known by the synonym of *Glauber's salt*, so named after John Rudolph Glauber, who published the process of manufacture in his work, "De Natura Salium," 1658. It is made by treating sodium chloride with sulfuric acid, and is, therefore, an intermediate product in the Leblanc process (p. 483).

Sodium sulfate occurs in efflorescent, monoclinic prisms of granular crystals possessing a bitter, saline taste. Its solubility in water is noteworthy, the following table showing its variations from 0 to 100° C.

At 0° C. 1 part crystalline sodium sulfate dissolves in 8 parts of water.
At 15° C. 1 " " " " " " 2.8 " " "
At 25° C. 1 " " " " " " 1 part " "
At 30° C. 1 " " " " " " 0.5 " " "
At 34° C. 1 " " " " " " 0.25 " " "
At 50° C. 1 " " " " " " 0.37 " " "
At 100° C. 1 " " " " " " 0.40 " " "

the temperature being, of course, that of the water.

From this table it will be noted that the maximum solubility is reached at 34° C., when 1 part of the salt (crystals) will dissolve in one quarter its weight of water. At 35° C. the solubility is 1 part in 0.3 part water, and from that to 100° C. the solubility slowly decreases. This phenomenon has been explained by claiming that up to 34° C. we deal with solution of the salt containing 10 molecules of water of crystallization. At 34° C. it is supposed that the salt loses 9 molecules of water, and from that time on we deal with a chemical possessing only 1 molecule of water of crystallization. The solution of sodium sulfate at 34° C. is a striking illustration of a supersaturated solution. Such a solution will remain intact if kept in a quiet place, even though the temperature of the solution be reduced below 33° C. If the flask is shaken, or even if the cork is removed, there will be a sudden formation of crystals, with the evolution of considerable heat, corresponding to the phenomenon of *retarded crystallization.* (See p. 145.) The crystallization due to agitation is not easy to understand. One explanation of why the crystallization takes place by merely removing the cork is that the air contains minute crystals of sodium sulfate, which, when the cork is removed, fall into the solution and act as nuclei.

Sodium sulfate is a useful purgative.

Dose.—15 Gm. (240 grains).

Sodii Sulfas Exsiccatus (N.F. VI), or *Exsiccated Sodium Sulfate,* represents Sodii Sulfas (U.S.P.) minus its 10 molecules of water of crystallization. It is used in making *artificial Carlsbad salt* of the Formulary (see p. 327).

Dose.—8 Gm.; (2 drachms).

Sal Carolinum Factitium (N.F.), or *Artificial Carlsbad Salt,* is mentioned here since sodium sulfate is its chief constituent, the other ingredients being sodium chloride and bicarbonate and potassium sulfate.

Sal Carolinum Factitium Effervescens (N F.) is an effervescent variety of the foregoing containing 25 per cent of the artificial salt made into effervescent granules with sodium bicarbonate and tartaric and citric acids (p. 327).

SODII THIOSULFAS—Sodium Thiosulfate

(Sod. Thiosulf.—"Sodium Hyposulfite")

$Na_2S_2O_3.5H_2O$. Molecular weight, 248.19

Sodium Thiosulfate, when rendered anhydrous by drying to constant weight at 100° C., contains not less than 99 per cent of $Na_2S_2O_3$. It contains not less than 32 per cent and not more than 37 per cent of water.

Storage.—Preserve in well-closed containers.

Summarized Description.

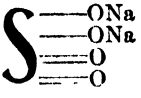
Colorless, large crystals or coarse crystalline powder; cooling, then bitter taste; efflorescent above 33° C.; soluble in about 0.5 part of water; insoluble in alcohol; dissociated on high heat to sulfur, sulfide, and sulfate. For details see U.S.P., p. 349.

For *tests for identity,* for *impurities* (sulfites, bisulfites, arsenic, heavy metals, calcium) and for *assay* see U.S.P., p. 349.

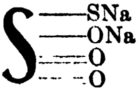
Remarks.—In the table of valences on p. 390 it will be found that the valence of sulfur is II, IV, and VI. As already learned, when an element has three valences and three oxides, the oxide showing the highest valence is given the termination "ic," while the oxide showing the lowest valence has "hypo" prefixed to the name of the positive element, whose termination becomes "ous." Under this rule, that oxide in which sulfur acts with the valence II should be termed hyposulfurous oxide, and the formula of this body is SO.

If hyposulfurous oxide be SO, then hyposulfurous acid will be $SO + H_2O$ or H_2SO_2, and sodium hyposulfite will be Na_2SO_2 (see p. 392) which is quite different from the formula given above; the so-called "sodium hyposulfite," $Na_2S_2O_3$, being really sodium thiosulfate. "*Thios*" is Greek for sulfur, hence the literal translation of thiosulfate is "sulfosulfate," a most appropriate title for the body $Na_2S_2O_3$, as is shown by the following comparison of the graphic formula of it with that of normal sodium sulfate:

SODIUM SULFATE



SODIUM THIOSULFATE



Sodium thiosulfate, $Na_2S_2O_3$, can be resolved into Na_2SO_3 (sodium sulfite) and sulfur, and inversely the thiosulfate can be made by boiling the sulfite with sulfur.

The commercial method of manufacture is by treating calcium thiosulfate with sodium sulfate, as shown in the following equation:

$$CaS_2O_3 + Na_2SO_4 = CaSO_4 + Na_2S_2O_3.$$

The calcium thiosulfate used in the above reaction is obtained from the calcium sulfide residue of the Leblanc process (p. 484). On exposure to air the calcium sulfide found therein is oxidized to calcium thiosulfate, which is lixiviated from the insoluble matter of the residue. Sodium thiosulfate is also made by cooking sulfur with sodium sulfite.

Sodium thiosulfate occurs in colorless, transparent crystals, soluble in less than 1 part of water. It is used largely in commerce, being a valuable antichlor in paper manufacture. It is the "hypo" of photographers, being used by them as a developer (see p. 624), it having the power of dissolving the chloride and bromide of silver. When brought in contact with an iodine solution, it immediately discharges the color of same, as explained on p. 427. The decolorizing influence of sodium thiosulfate on iodine is applied in the determination of the iodine strength of various pharmaceuticals, the same being titrated with decinormal solution of sodium thiosulfate. Sodium thiosulfate has been recommended as exhibiting all the therapeutic value of sulfur in a soluble form, it being stated, when a solution enters the stomach, the acids thereof throw out a sufficient amount of sulfur to become active. In the same way the ointment of sodium hyposulfite has been recommended in place of sulfur ointment. It is said to be of value as an antidote for hydrocyanic acid.

Dose.—1 Gm. (15 grains).

Sodii Bisulfis (U.S.P. VIII) is another of the acid salts described on p. 398. Being a bisulfite, it is a derivative of sulfur*ous* acid, which itself is derived from sulfurous oxide. This oxide shows sulfur with the valence IV, and its formula is SO_2, as is shown graphically on p. 389. $SO_2 + H_2O = H_2SO_3$, which is sulfurous acid. When all the hydrogen of sulfurous acid is replaced by sodium, we get sodium sulfite, Na_2SO_3, but when only one of the hydrogen atoms is replaced—by 1 atom of sodium—we get the bisulfite, $NaHSO_3$.

This salt is made by passing sulfurous acid gas through solution of sodium carbonate to saturation. The solution is then cooled, when the salt crystallizes out.

Sodium bisulfite is an unstable solid, rapidly losing sulfur dioxide and becoming oxidized to sulfate. For this reason it should be kept in a cool place, in small, well-stoppered bottles, which are to be completely filled. Sodium bisulfite is used as a reducing agent in organic chemistry, and is particularly valuable in the bleaching industry for the removing of the last traces of chlorine from the bleached fabric. Substances used for this purpose are known as *antichlors*. It is comparatively little used in medicine, but when so used, it is as an antiseptic. *Dose.*—500 mg. (7½ grains).

Sodii Chloras (U.S.P. VIII), $NaClO_3$, is made by treating calcium chlorate with sodium chloride.

It can also be made by treating potassium chlorate with sodium bitartrate by the following equation:

$$KClO_3 + NaHC_4H_4O_6 = KHC_4H_4O_6 + NaClO_3.$$

The potassium bitartrate produced in the reaction precipitates from the solution as it does in the Fothergill process (p. 454).

Sodium chlorate so closely resembles potassium chlorate that extended comment is unnecessary. Like potassium chlorate, it must be handled carefully in reference to trituration with oxidizable bodies, in order to avoid an explosion.

Its only advantage over potassium chlorate is that it is more soluble in water, 1 part of the sodium salt dissolving in 1.1 parts of water, while 1 part of potassium chlorate requires 16.5 parts of water to make a solution. Its uses are about the same as those of potassium chlorate. *Dose.*—250 mg. (4 grains).

Sodii Cyanidum (U.S.P. IX), NaCN, was introduced into the Pharmacopœia in 1916 to replace potassium cyanide at the time when potassium compounds were very scarce because of war conditions. It is made by the Bucher process by heating sodium carbonate and carbon to 900° C. and passing nitrogen over the heated mass; iron being used as catalyst.

Sodii Fluoridum, NaF, must be mentioned because of its large use as a restaurant insecticide. Its careless use in this way has been responsible for a number of poisoning cases. Its antidote is soluble calcium compounds, preferably intramuscular injections of calcium gluconate.

Sodii Glycerophosphas (N.F. VI) or *Sodium Glycerophosphate,* $C_3H_5(OH)_2PO_4Na_2$, is the sodium salt of glycerophosphoric acid (see p. 680) and is employed as a nutritive tonic. It is a constituent of *compound elixir of glycerophosphates* (N.F.). *Dose.*—250 mg. (4 grains).

Sodii Hypophosphis (N.F. VI) or *Sodium Hypophosphite,* $NaPH_2O_2$, is prepared in a manner similar to that for making potassium hypophosphite—by treatment of calcium hypophosphite with sodium carbonate.

Sodium hypophosphite occurs in the form of small transparent plates or chiefly in white, granular powder. It is soluble in 1 part of water and 30 parts of alcohol. Like all hypophosphites, the sodium hypophosphite must be heated with great care, as otherwise the following chemical reaction will occur:

$$5NaPH_2O_2 + \text{heat} = Na_4P_2O_7 + NaPO_3 + 2PH_3 + 2H_2,$$

the resulting gas *phosphine* (PH_2) being spontaneously combustible and producing an explosion.

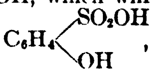
Sodium hypophosphite is a constituent of *syrup of hypophosphites* (N.F.). It may be here stated that hypophosphorous acid and hypophosphites act as reducing agents on silver and mercury compounds, hence the salts of these metals should not be prescribed with syrup of hypophosphites. Like all hypophosphites, the salt of sodium is used as a tonic and nutrient in wasting diseases. *Dose.*—500 mg. (8 grains).

Sodii Hyposulfis, Na_2SO_2 or $Na_2S_2O_4$, is mentioned as the true sodium hyposulfite. The salt commonly called by this name is in truth, sodium thiosulfate (p. 493). The true hyposulfite is now used quite largely as a reducing agent in the dye industry.

Sodii Nitras (U.S.P. VIII), $NaNO_3$, is a purified form of the native *Chile saltpetre.* Large deposits of this mineral are found in South America. The native ore is a combination of sodium nitrate with sodium iodate, and the latter chemical, as mentioned on p. 426, yields practically all the iodine in use in the world. The iodate is removed from the nitrate by crystallization in the district where mined, and is there worked into iodine (p. 426), while the nitrate is shipped into commerce practically free from iodide.

Sodium nitrate has become of tremendous general importance, since Chile saltpetre has been the chief fertilizer of the world. The possibility of exhaustion of the Chilean field caused scientists to sound a note of warning and attempts to make nitric acid and sodium nitrate synthetically were started. These syntheses, using the nitrogen of the air as the basis, are now accomplished by several methods which are grouped under the title "nitrogen fixation" (p. 446).

Sodium nitrate is the source of the commercial nitrates. It is rarely used in medicine, the potassium nitrate being preferred. When used, it is as a diuretic, as is potassium nitrate. *Dose.*—0.5 Gm. (8 grains).

Sodii Phenolsulfonas (U.S.P. IX), or *Sodium Sulfocarbolate,* has a complex formula, $NaSO_3C_6H_4OH$. This is the sodium salt of sulfocarbolic acid, which is made by treating phenol (or carbolic acid) with sulfuric acid, whereby one hydrogen of C_6H_5OH (see graphic formula on p. 775) is replaced by the group SO_2OH, which will be recognized as sulfuric acid, less one hydroxyl. This union gives us  $C_6H_4\begin{smallmatrix}\diagup SO_2OH\\ \diagdown OH\end{smallmatrix}$, sulfocarbolic acid, and the sodium in the salt replaces the hydrogen of the hydroxyl attached to the SO_2OH group.

Sodium sulfocarbolate is made by treating phenol with sulfuric acid, and letting stand for twenty-four hours, when sulfocarbolic acid is formed:

$$C_6H_5OH + H_2SO_4 = C_6H_4(SO_2OH)OH + H_2O.$$

To the acid mixture barium carbonate is added, thus forming barium sulfocarbolate, which is soluble, while the excess of sulfuric acid separates out as barium sulfate. To the filtered solution of barium sulfocarbolate, sodium carbonate is added, producing the following reaction:

$$Ba(SO_3C_6H_4OH)_2 + Na_2CO_3 = 2NaSO_3C_6H_4OH + BaCO_3.$$

The barium carbonate thus formed precipitates out and is separated by filtration from the solution of sodium sulfocarbolate, which is then concentrated by evaporation to a point where crystallization takes place.

Sodium sulfocarbolate occurs as transparent, colorless prisms, somewhat efflorescent, possessing a delicate pink tint. This coloration, however, is due to the same cause as is the pink color of phenol, and hence may possibly be considered as an impurity.

Sodium sulfocarbolate is used as an antiferment. *Dose.*—250 mg. (4 grains).

Sodii Pyrophosphas (U.S.P. VIII) or *Sodium Pyrophosphate*, $Na_4P_2O_7$, introduces us to an acid of phosphorus not yet considered—pyrophosphoric. On a preceding page (p. 481), under Borax, mention was made of the fact that the prefix "pyro-" indicates application of strong heat; this applies to pyrophosphoric acid.

On p. 396 the difference between true orthophosphoric acid, H_5PO_5, the so-called "orthophosphoric acid," H_3PO_4, and metaphosphoric acid, HPO_3, is graphically demonstrated, and mention is there made that all phosphoric acids are derived from phosphoric oxide, P_2O_5, a body in which phosphorus acts with valence v.

If to P_2O_5 we add 1 molecule of water, we get metaphosphoric acid, viz.,

$$P_2O_5 + H_2O = H_2P_2O_6 \text{ or } 2HPO_3;$$

and if we add 3 molecules of water to 1 molecule of phosphoric oxide, we get the official phosphoric acid, viz.,

$$P_2O_5 + 3H_2O = H_6P_2O_8 \text{ or } 2H_3PO_4.$$

Likewise, if we subtract 1 molecule of water from official phosphoric acid, we get metaphosphoric acid, viz.,

$$H_3PO_4 - H_2O = HPO_3.$$

If, on the other hand, we subtract 1 molecule of water from 2 molecules of official phosphoric acid, we get pyrophosphoric acid, as shown below:

$$\begin{array}{rl} 2H_3PO_4 = & H_6P_2O_8 \\ \text{Less 1 molecule of water or} & H_2\ O \\ \hline \text{Give pyrophosphoric acid} & H_4P_2O_7. \end{array}$$

The pyrophosphate is obtained by heating sodium phosphate until its solution no longer gives a yellow precipitate with silver nitrate.

Trisodium Phosphate, Na_3PO_4, is now being made on a commercial scale and its manufacture is protected by letters patent. It has been found to be of value as a detergent and as a water softener. Eschenbrenner has found that small quantities are efficient in masking the taste of veronal.

Sodium Phosphite, Na_2PHO_3, is made by treating sodium bicarbonate with solid phosphorous acid, the latter being produced by dropping phosphorus trichloride into water in a flask filled with carbon dioxide, thus excluding air. The phosphite is recommended as an antidote for mercuric chloride. (See p. 616.)

Sodium Silicate, $NaSiO_3$, was recognized in the Pharmacopœia of 1890 as a nearly saturated solution (*liquor sodii silicatis* or *liquid glass*). It is made by fusing together common sand and sodium carbonate in the presence of a small quantity of charcoal. The fused mass is poured into water in order to obtain the product in small porous masses, which are more readily soluble.

Sand is silicic oxide, SiO_2, an exact analogue to carbonic oxide, CO_2. Silicic oxide plus sodium carbonate gives us sodium silicate and gaseous carbonic oxide:

$$SiO_2 + Na_2CO_3 = Na_2SiO_3 + CO_2.$$

Solution of sodium silicate is a more or less transparent, but faintly yellowish, viscid liquid, the keeping of which is a source of considerable annoyance to the retail pharmacist. If kept in glass-stoppered bottles it will cause the stopper to stick to the neck. It usually is somewhat alkaline, and therefore attacks cork, and if not tightly corked, it will comparatively easily evaporate to a glassy mass, which is quite difficult to redissolve. This body is called *liquid glass* or *water glass*, because of its resemblance to ordinary glass, which is a combination of sodium silicate with the silicates of lead and calcium.

Liquid glass forms, on drying, a vitreous coating which is hard and inflexible. Accordingly, it is used in mending fractured limbs, as is also plaster of paris, the broken member being swathed with bandages which are fixed firmly in their place by applications of the liquid glass. After standing, the solution solidifies to a hard, rigid mass, which securely and firmly encases the limb.

It is superior to plaster of paris in the greater ease with which the glass dressing can be removed after the limb is set.

The plaster has to be chipped off—a very tiresome operation; the glass, on the other hand, can be dissolved off with hot water.

It is found, however, that liquid glass sets too slowly for the average operation, and plaster-of-paris settings are, therefore, usually preferred.

Large quantities of liquid glass are now used in agricultural districts for preserving eggs which are coated with the solution thus excluding the putrefactive organisms found in the air. Used for many years as an adulterant of common soap, it has latterly come into its own as useful commercial detergent.

Sodii Sulfis, Na_2SO_3, is made by passing sulfur dioxide gas, produced in the way as explained under sulfurous acid (p. 456), into a solution of sodium carbonate, and then evaporating the solution. The *exsiccated* form was recognized by U.S.P. IX. It is in the form of a white powder soluble in 3.2 parts of water. It is used as an antiferment. *Dose.*—1 Gm. (15 grains).

BIBLIOGRAPHY

Sodium.—(History) Thorpe, Ch. News, 97, 1908, 193 and 210; Lucas, Ch. and Dr., 84, 1914, 904; Hackh, A.J.P., 90, 1918, 573; Dyson, Ph. Jl., 127, 1931, 42. (Isolation) Anon., Am. Dr., 14, 1886, 165; Castner, Ch. News, 54, 1886, 218; Jl. Soc. Ch. Ind., 10, 1891, 777; Botsford, Ch. Met. Eng., 26, 1922, 888 and 932. (Production and uses) Holmsen, C.A., 20, 1926, 1695; Anon., Jl. Soc. Ch. Ind., 48, 1929, 835; Anon., A.J.P., 102, 1930, 416. (Properties) Richards and Brink, Jl. Am. Ch. Soc., 29, 1907, 117. (Tests) Anon., Merck's Rep., 14, 1905, 350; Bottger, Jl. Soc. Ch. Ind., 48, 1929, 681.

Sodium Hydroxide.—(Manufacture) Anon., Met. Ch. Eng., 13, 1915, 514; Anon., Ch. and Dr., 89, 1917, 961 (Electrolytic soda) Junkersfeld, C.A., 11, 1917, 315; Pritchard and Gollup, Jl. Soc. Ch. Ind , 44, 1925, 220 to 243; Moore, *ibid.*, 44, 1925, 1085; Kolb, C.A., 23, 1929, 4302.

Sodium Peroxide.—Anon., Jl. Soc. Ch. Ind., 44, 1925, 498.

Sodium Benzoate.—(Manufacture and uses) Dowler, A.J.P., 29, 1857, 314; Klebs and Schlickum, A.Ph.A , 27, 1879, 462.

Borax.—(History) Harris, Jl. A.Ph.A , 7, 1918, 858; Edit., Jl. Soc. Ch. Ind., 52, 1933, 151. (Source) Anon., Am. Dr., 28, 1896, 46; Hake, Jl. Soc. Ch. Ind., 8, 1889, 854; Dupont, Jl. Ind. Eng. Ch., 2, 1910, 500; Anon., C A., 4, 1910, 1283; Robiquet and Marchand, Jl. de ph., 4, 1818, 97. (Structure) Wiberg, C.A., 24, 1930, 4477. (Properties and tests) Hoffmann, C.A., 11, 1917, 2945; Bancroft and Nugent, C.A., 23, 1929, 3618.

Dobell's Solution.—Anon., Dr. Circ., 73, 1929, 71; Bauer, Jl. A.Ph.A , 19, 1930, 475

Perborates.—Melikoff and Pissarjevsky, B., 31, 1898, 678; Fuhrmann, Ch. Zt., 35, 1911, 1022; Foregger, Am. Dr., 48, 1906, 39 and 155; Ligor, Am. Dr., 62, 1914, 370; Foerster, C.A., 15, 1921, 3595; Alsgaard, C.A., 15, 1921, 3947; Furness, Jl. Soc. Ch. Ind., 44, 1925, 1242.

Sodium Bromide.—(Temperature on dissolving) Hemm, Meyer Bros. Drug, 31, 1910, 199. (Medical uses) Scheepe, C.A., 20, 1926, 449.

Sodium Carbonate.—(History) Anon., Jl. Soc. Ch. Ind., 42, 1923, 27 and 384. (Leblanc process) Lunge, Sulphuric acid and alkali, 2, 300; Ost, Zt. angew. Ch., 20, 1907, 1689; Pritchard, Jl. Soc. Ch. Ind., 47, 1928, 57; Furness, *ibid.*, 48, 1929, 3; Dunn, *ibid.*, 50, 1931, 985. (Solvay process) Mond, Jl. Soc. Ch. Ind., 4, 1885, 527; Pennock, Jl. Am. Ch. Soc., 28, 1906, 1242; Vanzetti, Ch. Zt., 27, 1903, 229; Mason, C.A., 8, 1914, 2924; Jurisch, C.A., 9, 1915, 2429; Ciochina, C.A., 19, 1925, 3002; Little, Jl. Soc. Ch. Ind., 48, 1929, 202T. (Cryolite process) H. B., Ch. News, 9, 1864, 111; Lunge, Ch. News, 12, 1865, 158; Holland, Jl. Ind. Eng. Ch., 3, 1911, 63 (Natural soda) Coates, Jl. Soc. Ch. Ind., 43, 1924, 872; Anon., *ibid.*, 43, 1924, 1000; Robertson, Jl. Ind. Eng. Ch., 23, 1931, 478. (Hydrochloric acid "rain") Anon., A.J.P , 25, 1853, 39. (Sodium aluminate) Hantzsch, Zt. anorg. Ch., 30, 1902, 296; Herz, Zt. anorg. Ch., 25, 1900, 155; Slade, C.A., 5, 1911, 3363; Mahin, 8th Int. Cong. App. Chem., 22, 1922, 207; Hackh, A.J.P., 95, 1923, 552.

Sodium Bicarbonate.—(Structure) Bicher, Ph. Jl., 85, 1910, 365. (Incompatibilities) Ricciardelli, C.A., 18, 1924, 440.

Sodium Chlorate.—(Manufacture) Bottomley and Molesworth, Pat. 3005 (1881), Thorpe Dict., 2, 1912, 35. (Solubility) Bell, Jl. Soc. Ch. Ind., 42, 1923, 1218A. (Toxicity) Strzyzowski, C.A., 25, 1931, 5711.

Sodium Chloride.—(Source) Anon., A.Ph.A., 39, 1891, 503; Anon., A.J.P., 35, 1863, 557; Arthur, C.A., 14, 1920, 716; Edit., Jl. Ind. Eng. Ch., 18, 1926, 883; Anon., Ph. Era, 67, 1930, 278. (Properties) Anon., Jl. Soc. Ch. Ind., 41, 1922, 979A; Przibram, C.A., 24, 1930, 1295; Wille, *ibid.*, 26, 1932, 3165. (Normal saline) Engelmann, A.Ph.A., 51, 1903, 636. (Poisonous character) Barlow, Jl. A.Ph.A., 2, 1913, 104.

Sodium Fluoride.—(Toxicity) Sharkey and Simpson, A.J.P., 105, 1933, 38.

Sodium Citrate.—(Medical uses) Rosenthal, Ph. Jl., 103, 1919, 537; Neuhoff and Hirschfeld, C.A., 15, 1921, 899; Rifo, C.A., 24, 1930, 893.

Sodium Cyanide.—(Manufacture) Sadtler, A.J.P., 95, 1923, 281; Guernsey and Sherman, Jl. A.C.S., 47, 1925, 1933.

Sodium Hypophosphite.—Trommsdorf, A.J.P., 32, 1860, 87; Anon., Ph. Jl., [3], 8, 1877, 86.

Sodium Iodide.—(Manufacture) Anon., C.A., 19, 1925, 1180. (Medical uses) Marine and Others, Jl. A.M.A., 72, 1919, 18731 and 75, 1920, 674; Osborne, *ibid.*, 79, 1922, 615; McClendon, Science, 55, 1922, 358.

Sodium Nitrate.—(Chile saltpetre) Anon., A.J.P., 24, 1852, 225; Barrett, N. Y. Times, Feb. 23, 1913, p. 8; Duncan, Chemistry of Commerce, 1907, 47; Lerna, Ch. Eng., 10, 1909, 1; Blumenfeld, C.A., 7, 1913, 1100; Anon., Ch. and Dr., 77, 1915, 46; Cuevas, A.J.P., 88, 1916, 189; Hobsbaum and Grigiani, Dr. Circ., 61, 1917, 132; Ossa, C.A., 16, 1922, 317; Hamid, Jl. Soc. Ch. Ind., 47, 1928, 481B; Anon., *ibid.*, 48, 1929, 272; Delcourt and co-workers, C.A., 23, 1929, 3053; Donald, *ibid.*, 25, 1931, 5957; Curtis, Jl. Ind. Eng. Ch., 23, 1931, 456.

Sodium Nitrite.—(Manufacture) Darbon, Ch. Zt., 23, 1899, 173. (Pharmacology) Dossin, C.A., 6, 1912, 1932. (Properties) Gangloff, Jl. Ind. Eng. Ch., 12, 1920, 613. (Incompatibility) Luff and Finnemore, Dr. Circ., 60, 1916, 21.

Sodium Phenolsulfonate.—(Manufacture) Procter, A.J.P., 42, 1870, 131.

Sodium Phosphate.—(Structure) Reynolds, Ph. J.., [3], 8, 1877, 84. (Manufacture) Berzelius, Gmelin-Kraut, 2^1, 1906, 391. (Arsenic in it) Bird, Ch. and Dr., 56, 1900, 1073; Gane, Am. Dr., 37, 1900, 101. (Compound solution) Horn, Merck's Rep., 20, 1911, 71; Norwood, Dr. Circ., 58, 1914, 390.

Sodium Biphosphate.—Jordan, C. A., 7, 1913, 3789; Abraham and Rae, Ph. Jl., 114, 1925, 54.

Trisodium Phosphate.—(Manufacture) Carothers, U. S. Pat. 1,689,547, 1928; Snell Jl. Ind. Eng. Ch., 23, 1931, 470. (Uses) Vuilleumier, 24, 1930, 267; Eschenbrenner, Pract. Dr., 48, Apr., 1930, 33; Kroemer, Ch. Zt., 56, 1932, 411 and 722.

Sodium Pyrophosphate.—Balareff, C.A., 9, 1915, 276 and 11, 1917, 2645; Partington and Wallsom, C.A., 22, 1928, 1553.

Sodium Phosphite.—Linhart, C.A., 11, 1917, 2527.

Sodium Salicylate.—(Discoloration) Greenish and Beesley, Ph. Jl., 94, 1915, 201; Macadie, *ibid.*, 94, 1915, 1355; Krantz, Jl. A.Ph.A., 17, 1928, 1203 and 18, 1929, 1250; Davies, C.A., 22, 1928, 2507; Daŭbert, Merck's Rep., 39, 1930, 14; Grill, Jl. A.Ph.A., 21, 1932, 765.

Glass.—(History) Anon., Spatula, 16, 1910, 594; Anon., A.Ph.A., 59, 1911, 31.

Sodium Silicate.—(Uses) Baker, Jl. Ind. Eng. Ch., 23, 1931, 1025. (Manufacture) Deckert, Jl. Soc. Ch. Ind., 45, 1926, 786.

Sodium Sulfate.—(History) Anon., Pharm. Era, 52, 1919, 263; Darmstaedter, Ch. Zt., 50, 1926, 585. (Structure) Bunte, B., 7, 1874, 646. (Manufacture) Glauber, Kopp, 4, 1847, 40; Il'inskii, C.A., 22, 1928, 3739. (Physical properties) Thomsen, Am. Dr., 16, 1887, 50; Loewel, Ann. de chim. et phys., [3], 29, 1850, 62; Ostwald, Principles, 1902, 483. (Medical action) Dreyer, C.A., 22, 1928, 3932.

Sodium Thiosulfate.—(Structure) Spring, B., 7, 1874, 1158; Ray, C. A., 25, 1931, 5637. (Manufacture) Schaftner, Ch. News, 20, 1869, 96; Leripg, A.J.P., 18, 1847, 78; Hargreaves and Dunningham, Jl. Soc. Ch. Ind., 42, 1923, 147T. (Therapeutics) Lunan, Ph. Jl., 110, 1923, 384; Hug, C.A., 27, 1933, 135.

Sodium Hyposulfite, True.—(Manufacture) Pratt, Jl. Ind. Eng. Ch., 16, 1924, 676; Zhivotinskii, C.A., 26, 1932, 5261.

CHAPTER XXVII

LITHIUM AND AMMONIUM

LITHIUM

Symbol, Li. Atomic weight, approximately 7

THE word lithium is derived from the Greek "*lithos*," meaning "stone," being so named by Berzelius because found in minerals. The presence of the new element was first detected by Arfvedson in 1817, but its isolation in more than traces was not accomplished until 1855, when Bunsen and Mattiessen obtained it by electrolysis of fused lithium chloride.

The chief ores of lithium are *lepidolite* and *spodumene*, combinations of the silicates of lithium, sodium, and aluminum, and *triphylite*, which is a mixture of the phosphates of lithium, sodium, iron, manganese, and calcium.

It was first discovered in mineral water by Berzelius (1822), who noted its presence in Carlsbad water.

It is also found in tobacco and in the sugar beet.

The metal cannot be isolated by chemical means, such as are used in obtaining sodium and potassium, by reason of the nonvolatile character of the metal, but is prepared only by electrolysis of the chloride.

Lithium is the lightest of all metals, having the specific gravity 0.534, *i. e.*, it has less than six tenths the weight of water, and is lighter than petroleum or ether, and hence floats on both of these liquids. It is a soft, silvery-white metal, possessing characteristics similar to that of the other members of the group (sodium and potassium), although being less active chemically. Thus, while it reacts in water with the formation of lithium hydroxide, it does not do so with the explosive violence that characterizes the same reaction in the case of sodium and potassium.

The most characteristic test for lithium is the crimson color which it or its salts transmits to a colorless flame which is so sensitive that $^{1}/_{100,000}$ mg. of lithium in 1 cc. of water can be thus detected. If the solution of the chloride be treated with ammonium carbonate, the rather sparingly soluble carbonate is precipitated. This carbonate is somewhat soluble in water, however (1 part in 75 parts water), hence the statement already made (p. 458) that the carbonates of the alkalis dissolve in water still obtains.

No salts of lithium are recognized in U.S.P. XI. U.S.P. IX described the following:

Lithium bromide, 85 per cent absolute $LiBr$.
Lithium carbonate, 98.5 per cent absolute Li_2CO_3.
Lithium citrate, 98.5 per cent absolute $Li_3C_6H_5O_7.4H_2O$.

Lithii Bromidum (N.F. VI), or *Lithium Bromide*, $LiBr$, is made by treating lithium carbonate with potassium bromide, as shown in the following equation:

$$Li_2CO_3 + 2KBr = K_2CO_3 + 2LiBr,$$

or by treating lithium sulfate with potassium bromide. In both cases the potassium salt—the carbonate or the sulfate—is precipitated from the lithium bromide solution by the addition of a small quantity of alcohol. Yvon's process of preparation is by treating lithium carbonate with bromine and then passing hydrogen sulfide through the mixture until the color of the bromine has disappeared. In this case the sulfide acts on the bromine to form hydrobromic acid and sulfur, the latter precipitating. The hydrobromic acid, in turn, acts on the lithium carbonate to form lithium bromide, and the result of the reaction is a solution of lithium bromide containing a precipitate of sulfur, which is removed by filtration. The filtered liquid is concentrated by evaporation and crystallized by desiccation, under the bell glass, with sulfuric acid. A fourth process suggested is by treating ferrous bromide with lithium carbonate, and is, therefore, similar to the process for making potassium bromide. (See p. 465.)

Lithium bromide is a white deliquescent granular salt, soluble in 0.6 part of water. It is used as hypnotic in rheumatic troubles. *Dose.*—1 Gm. (15 grains).

Lithii Benzoas (N.F. VI) or *Lithium Benzoate*, $LiC_7H_5O_2$, is made by treating lithium carbonate with benzoic acid, as shown in the following equation:

$$Li_2CO_3 + 2HC_7H_5O_2 = 2LiC_7H_5O_2 + H_2O + CO_2.$$

It occurs in a light white powder or small, shiny scales, and is used as a diuretic and as a remedy for gout. *Dose.*—1 Gm. (15 grains).

Lithii Carbonas (N.F. VI) or *Lithium Carbonate*, Li_2CO_3, is prepared from lepidolite by making a paste of the finely powdered ore with concentrated sulfuric acid, calcining, and treating the residue with water. This throws out silicic acid, and converts the metals into sulfates, which go into solution. To the solution, potassium sulfate is added, when, on concentration, the aluminum crystallizes out as alum. To the remaining solution of the sulfates of sodium, potassium, and lithium, sodium carbonate is added, when crude lithium carbonate precipitates. This is purified by cooking with milk of lime or with aluminum hydroxide, when a solution of lithium hydroxide results, and from this the carbonate is produced by use of sodium carbonate. Lithium carbonate is also made by adding the chloride to warm 20 per cent ammonium carbonate solution, or to a solution of ammonium carbonate containing ammonia water.

Lithium carbonate is a light white powder, soluble in about 78 parts of water. It is used in gout because it is supposed to exert a solvent action upon uric acid. *Dose.*—500 mg. (8 grains).

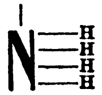
Lithii Citras (N.F. VI) or *Lithium Citrate*, $Li_3C_6H_5O_7$, is made by treating the lithium carbonate with citric acid, and crystallization of the citrate by evaporation of the solution and occurs in white, deliquescent powder or granules, soluble in about 1.4 parts of water. Its use is the same as that of the carbonate, but has the advantage of possessing a less disagreeable taste, and is more easily tolerated by the stomach. *Dose.*—500 mg. (8 grains).

Sal Lithii Citras Effervescens (N.F. VI), or *Effervescent Lithium Citrate*, is a 5 per cent mixture of lithium citrate with sodium bicarbonate, dried tartaric acid, and crystalline citric acid, granulated by softening the mass with heat and rubbing through a coarse sieve.

Lithii Salicylas (N.F. VI) or *Lithium Salicylate*, $LiC_7H_5O_3$, is prepared by treating lithium carbonate with salicylic acid, heating until the effervescence ceases, and then granulating. The salt occurs in the form of a grayish-white, deliquescent powder, having a sweetish taste, very soluble in both alcohol and water. Lithium salicylate is a popular remedy for rheumatism and gout, since it possesses the antirheumatic properties of both salicylic acid and lithium. *Dose.*—1 Gm. (15 grains).

AMMONIUM

Ammonium is discussed as an element, although we know it is a compound and have no proof that it exists in a free state. By ammonium we mean the radical NH_4. Graphically,



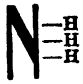
The discussion of radicals found on pp. 633, 634 will explain how NH_4, with one free bond, can act like a metal with one free bond.

The only inkling we have of the metallic character of ammonium and the possibility of its eventual isolation comes from the fact that, by electrolysis of ammonium hydroxide in the presence of mercury, there is formed an amalgam of ammonium with mercury similar to that yielded by metallic sodium or potassium with the same liquid element.

This amalgam, on being heated, splits into mercury, ammonia (NH_3), and hydrogen.

Schlubach and Ballauf working at low temperatures are convinced that the radical, NH_4, is existent under proper physical conditions.

Do not confound *ammonium* with *ammonia*. Ammonia is a gas of sharp, penetrating odor, characteristic of spirit of hartshorn, having the formula NH_3, or, graphically,



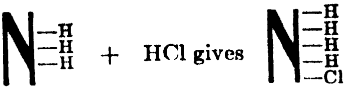
It is a definite chemical in which all three of the nitrogen bonds are satisfied by hydrogen. Ammonium is a radical, showing nitrogen with five bonds and only four of these taken up by hydrogen, leaving one free bond ready for action. The formation of ammonium compounds from ammonia is different from metallic combinations. If we treat a metal—say, potassium—with hydrochloric acid, hydrogen is evolved and a chloride is formed, thus—

$$K + HCl = KCl + H.$$

If, on the other hand, we treat ammonia with hydrochloric acid, ammonium chloride is formed without evolution of hydrogen, thus—

$$NH_3 + HCl = NH_4Cl,$$

or, graphically,



$$N\begin{matrix}-H\\-H\\-H\end{matrix} + HCl \text{ gives } N\begin{matrix}-H\\-H\\-H\\-H\\-Cl\end{matrix}$$

Again, let it be reiterated that *sodium* (Na) is not *soda* (NaOH), *potassium* (K) is not *potash* (KOH), and *ammonium* (NH_4) is not *ammonia* (NH_3).

Ammonia, as just mentioned, is a gas having the formula of NH_3. This body is interesting as one of the few volatile alkalis (the others being organic chemicals), and its presence in compounds is generally detected by means of its volatility, the suspected substance being treated with soda or potassa and heated; if ammonium compounds are present, the ammonia gas is evolved, and is readily recognized by its characteristic odor. If only minute quantities of the gas are evolved, it can be detected by means of moistened red litmus paper, which will turn blue upon being applied to the vapors of ammonia. When ammonia gas comes in contact with hydrochloric acid, white fumes of ammonium chloride are formed. In testing for minute quantities of ammonia, Nessler's reagent is employed. This consists of a solution of mercuric iodide in an excess of mercuric chloride, and when this colorless or faintly straw-colored liquid is added to the solution containing ammonia, the liquid is then changed to either an amber tint or a red-brown precipitate is produced, according to the amount of ammonia present. By this means small quantities of ammonia (even 1 part to 10,000,000), can be detected in a liquid.

The test is too sensitive for application in ordinary analytic processes, but is invaluable in detecting ammonia in drinking water, as already explained on p. 415.

Ammonia gas was first prepared by Priestley, in 1774, by heating ammonium chloride with slaked lime, the reaction being:

$$2NH_4Cl + Ca(OH)_2 = CaCl_2 + 2NH_3 + 2H_2O.$$

The evolved gas he called "alkaline air," the word ammonia (or Ammoniack) being first applied to it by Bergman in 1782.

Commercial ammonia gas is made from the ammoniacal liquor of gas works. In the manufacture of illuminating gas from coal the gas, as it leaves the retort, is passed through diluted sulfuric acid to remove the ammonia produced from the coal. In this way the acid liquid eventually becomes a solution of ammonium sulfate, and the crude sulfate obtained by evaporation of the solution is sold to the chemical manufacturers. By treating this crude sulfate with slaked lime the ammonia gas is evolved, and on being passed into water, forms the commercial solution of ammonia.

Ammonia is now made synthetically from the nitrogen of the air, affording another method of nitrogen fixation (see p. 446). Haber in Germany and Claude in France have devised workable processes in which the gases nitrogen (from the air) and hydrogen (from coke ovens or other sources) are submitted to great heat and pressure in steel tubes containing a catalyst. The catalysts employed are iron, uranium, molybdenum and tungsten in a state of fine subdivision. Sodium cyanide produced by the Bucher process (see p. 495) upon treatment with steam is broken up with the formation of ammonia.

AQUA AMMONIÆ—Ammonia Water

(Aq. Ammon.—Solution of Ammonium Hydroxide)

Ammonia Water is an aqueous solution of ammonia (NH_3) containing, in each 100 cc., not less than 9 Gm. and not more than 10 Gm. of NH_3. This solution deteriorates rapidly in open containers.

Storage.—Preserve in a cool place, in glass-stoppered or rubber-stoppered bottles made of hard glass, free from lead.

Condensed Recipe.

Dilute 398 cc. of stronger ammonia water with enough distilled water to make 1000 cc.

Summarized Description.

Colorless liquid; pungent odor; caustic, alkaline taste; fumes, when brought near concentrated hydrochloric acid; sp. gr. 0.957. For details see U.S.P., p. 63.

For *tests for identity*, for *impurities* (readily oxidizable matter, heavy metals, non-volatile matter) and for *assay* see U.S.P., p. 63.

Dose.—1 cc. (15 minims).

AQUA AMMONIÆ FORTIOR—Stronger Ammonia Water

(Aq. Ammon. Fort.)

Stronger Ammonia Water is an aqueous solution of ammonia (NH_3), containing not less than 27 per cent and not more than 29 per cent by weight of NH_3. This solution deteriorates rapidly in open containers.

Caution.—Great care should be used in handling the liquid because of its caustic and irritating properties.

Storage.—Preserve in a cool place, in glass-stoppered or rubber-stoppered bottles made of hard glass, free from lead.

Summarized Description.

Colorless liquid; very strong odor; very caustic; strongly alkaline; sp. gr. 0.897. For details see U.S.P., p. 63.

For *tests for identity* and for *impurities*, see ammonia water. For *assay* see U.S.P., p. 63.

Remarks.—It will be seen that the Pharmacopœia recognizes two strengths of ammonia water—the ordinary, containing about 10 per cent, by weight, of ammonia gas, and the stronger water, which contains about 28 per cent of the same gas and represents a saturated solution. Unfortunately, ammonia is not always sold by percentage of ammonia gas, but by the arbitrary marking of degrees.

The "degrees" mean the graduations of the Baumé scale of light liquids (see p. 61), and must not be confounded for the percentage. Thus 17° ammonia, largely sold by wholesalers, does not contain 17 per cent ammonia gas, but represents the specific gravity of 0.953, which means only 11½ per cent ammonia gas.

To render the subject still more vague, some wholesalers substitute for degrees Baumé arbitrary markings "F," "FF," "FFF," and even "FFFF." Presumably the first stands for "fortis" (strong), the second for "fortior" (stronger), and the third for "fortissimus" (strongest). In this case 4 F is outdoing the superlative.

When ammonia gas is run into water, ammonium hydroxide is produced by a reaction similar to that just cited as occurring between ammonia and hydrochloric acid. The reaction is:

$$NH_3 + HOH = NH_4OH,$$

the valence of nitrogen changing from III to V during the process.

According to Moore, a centinormal solution of ammonia contains 51 per cent present as NH_4OH, 45 per cent as NH_3 and 4 per cent as ammonium ions. Tommasi and other investigators, on the other hand, consider ammonia water as a solution of NH_3 in water.

Ammonia water (10 per cent) is called *spirit of hartshorn* because originally made by the destructive distillation of the horn of the hart (*cornu cervi*). Regarding the stronger ammonia water, containing 28 per cent of ammonia gas, nothing need be added to what has already been said on p. 195.

Spiritus Ammoniæ (U.S.P. VIII), or *Spirit of Ammonia,* is an alcoholic solution of ammonia containing 10 per cent of the gas. The recipe of the former Pharmacopœia directed that the gas driven off from stronger ammonia water by heat be passed into alcohol; a procedure that the writer found both cumbersome and useless; since it was almost impossible to so obtain a 10 per cent product.

Linimentum Ammoniæ (N.F. VI) is discussed on p. 291.

Spiritus Ammoniæ Anisatus is a preparation in considerable demand in German neighborhoods. A recipe for it is given in N.F. VI. (See p. 206.)

AMMONIUM SALTS

Ammonium salts all contain the radical NH_4, which acts very much like the elements sodium and potassium. Thus, while the formula of sodium bromide is NaBr, so the formula of ammonium bromide is NH_4Br; as the formula of potassium sulfate is K_2SO_4, so that of ammonium sulfate is $(NH_4)_2SO_4$.

The following ammonium salts and their preparations are official:

Solution of ammonium acetate containing about 7 per cent	$NH_4C_2H_3O_2$.
Ammonium benzoate 98 per cent absolute	$NH_4C_7H_5O_2$.
Ammonium bromide 99 per cent absolute	NH_4Br.
Ammonium carbonate varying proportions of	NH_4HCO_3 and $NH_4NH_2CO_2$.
Aromatic spirit of ammonia. A pharmaceutical.	
Ammonium chloride 99.5 per cent absolute	NH_4Cl.
Ammonium salicylate 98 per cent absolute	$NH_4C_7H_5O_3$.

LIQUOR AMMONII ACETATIS—Solution of Ammonium Acetate

(Liq. Ammon. Acet.)

Solution of Ammonium Acetate contains, in each 100 cc., not less than 6.5 Gm. and not more than 7.5 Gm. of $CH_3.COO.NH_4$, with small amounts of acetic and carbonic acids.

Caution.—Only a recently prepared solution of ammonium acetate should be dispensed.

Condensed Recipe.

Dissolve 5 Gm. ammonium carbonate, in hard translucent pieces, in sufficient diluted acetic acid to make 100 cc. There is also given an alternative process; 50 Gm. ammonium carbonate are dissolved in water to make 500 cc.; 160 cc. acetic acid are diluted with water to make 500 cc.; equal volumes of the two solutions are mixed on dispensing. For details see U.S.P., p. 204.

Summarized Description.

Clear, colorless liquid, mildly saline, acidulous taste; acid reaction. For details see U.S.P., p. 204.

For *tests for identity*, for *impurities* (nonvolatile matter) and for *assay* see U.S.P., p. 205.

Remarks.—This solution, which contains about 7 per cent of the salt, and which is known by the synonym of *spirit of Mindererus*, is made by adding 5 Gm. of ammonium carbonate to 100 cc. of diluted acetic acid, and the Pharmacopœia directs that it should be freshly prepared when desired. The object of directing its being fresh is in order that the product will reach the patient in a slightly effervescent form, although the pharmacist must be careful not to cork the bottle while there is sufficient effervescence to produce an explosion. The alternative process of the present Pharmacopœia (which was also in U.S.P. 1880) is a much more convenient method of dispensing this preparation.

Solution of ammonium acetate is a refreshing refrigerant.

Dose.—15 cc. (4 fluidrachms).

AMMONII BENZOAS—Ammonium Benzoate

(Ammon. Benz.)

$NH_4C_7H_5O_2$. Molecular weight, 139.08

Ammonium Benzoate, when dried for twenty-four hours over sulfuric acid, contains not less than 98 per cent of $C_6H_5.COO.NH_4$.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Thin, white, laminar crystals or crystalline powder; loses ammonia on exposure to air; bitter saline, then acrid taste; soluble in about 10 parts of water, in about 29 parts of alcohol and in about 10 parts of glycerin; dissociates on heating into ammonia and benzoic acid, which volatilize. For details see U.S.P., p. 52.

For *tests for identity*, for *impurities* (heavy metals) and for *assay* see U.S.P., p. 52.

Remarks.—This official is made by treating ammonia water with a molecular quantity of benzoic acid. There must, however, be a slight excess of ammonia, as the acid benzoate is less soluble than the official salt. It occurs in four-sided crystals, soluble in 10 parts of water, and is used as a diuretic.

Dose.—1 Gm. (15 grains).

AMMONII BROMIDUM—Ammonium Bromide

(Ammon. Brom.)

NH_4Br. Molecular weight, 97.96

Ammonium Bromide, when dried for twenty-four hours over sulfuric acid, contains not less than 99 per cent of NH_4Br.

Storage.—Preserve in air-tight containers.

Summarized Description.

Colorless, hygroscopic, prismatic crystals or white, granular powder; pungent, saline taste; soluble in about 1.3 parts of water and in about 9.7 parts of alcohol; volatilizes on heating. For details see U.S.P., p. 53.

For *tests for identity*, for *impurities* (iodide, bromate, iron, barium, sulfates, heavy metals, nonvolatile matter) and for *assay* see U.S.P., p. 53.

Remarks.—This salt is made in several ways: first by treating the ammonium sulfate with potassium bromide, and precipitating out the potassium sulfate thus formed, by the addition of alcohol; secondly, by treating ferrous bromide with ammonia water, and filtering the resulting ferric hydrate, and concentrating the filtered solution of ammonia bromide. Dr. Pile's process is by treating bromine with ammonia water, as shown in the following equation:

$$6Br + 8NH_3 = 6NH_4Br + N_2.$$

The bromine must be placed in a stone jar, with four times its weight of water, the ammonia gas being added very gradually to the mixture until the solution is free from the odor of bromine. Too much stress cannot be laid on the care required in adding ammonia water, as the rapid addition of ammonia may result in the formation of a very explosive nitrogen bromide (NBr_3).

Ammonium bromide is used as a hypnotic.

Dose.—1 Gm. (15 grains).

AMMONII CARBONAS—Ammonium Carbonate

(Ammon. Carb.)

Ammonium Carbonate consists of ammonium acid carbonate (NH_4HCO_3) and ammonium carbamate ($NH_2.COO.NH_4$) in varying proportions, and yields not less than 30 per cent and not more than 32 per cent of NH_3.

For medicinal purposes, use only translucent pieces of ammonium carbonate.

Storage.—Preserve in air-tight containers, in a cool place and protected from light.

Summarized Description.

White, hard, striated, translucent masses; ammoniacal odor and taste; exposed to air, loses both ammonia and carbon dioxide, effloresces and falls to a white powder; volatilizes without charring, soluble in about 4 parts of water; decomposed by hot water. For details see U.S P., p. 54.

For *tests for identity*, for *impurities* (heavy metals, sulfate, thiosulfate, chloride empyreumatic matter) and for *assay* see U.S.P., p. 54.

Ammonium carbonate is not a true carbonate, the formula of which would be $(NH_4)_2CO_3$, analogous to Na_2CO_3. The official salt is the combination of ammonium bicarbonate $(NH_4)HCO_3$ (analogous to $NaHCO_3$), with ammonium carbamate. This carbamate is a complex substance, the derivation of which is here given as a matter of general interest.

Let us place side by side the graphic formulas of carbon dioxide, carbonic acid, and urea, a constituent of the urine, which has historic interest as the first organic substance that was made synthetically:

Carbon dioxide
CO_2

$$\mathrm{C}\begin{cases} =\mathrm{O} \\ =\mathrm{O} \end{cases}$$

Carbonic acid
H_2CO_3

$$\mathrm{C}\begin{cases} =\mathrm{O} \\ -\mathrm{OH} \\ -\mathrm{OH} \end{cases}$$

Urea
$CO(NH_2)_2$

$$\mathrm{C}\begin{cases} =\mathrm{O} \\ -\mathrm{NH_2} \\ -\mathrm{NH_2} \end{cases}$$

Carbamic acid is half-way between carbonic acid and urea, its graphic formula being—

$$\mathrm{C}\begin{cases} =\mathrm{O} \\ -\mathrm{OH} \\ -\mathrm{NH_2} \end{cases}$$

or HNH_2CO_2. Therefore, ammonium carbamate is $NH_4NH_2CO_2$.

This is the first carbonate we have discussed that deviates from the theoretic formula, such as can be developed by the method given on p. 399. We find, however, that there are several other official carbonates that are irregular as to formulas, and among them may be cited the carbonates of magnesium, zinc, and bismuth.

The official ammonium carbonate can be converted into the true carbonate by dissolving in water containing ammonia.

If we take ammonium bicarbonate..........................	NH_4HCO_3
and add to it ammonia.............................	NH_3
	$NH_4NH_4CO_3$
we get neutral ammonium carbonate..................	or $(NH_4)_2CO_3$
Likewise, if we take ammonium carbamate..............	$NH_4NH_2CO_2$
and add to it water................................	H_2O
we get neutral ammonium carbonate	$NH_4NH_4CO_3$ or $(NH_4)_2CO_3$.

Official ammonium carbonate can also be considered as $(NH_3)_3(CO_2)_2$, H_2O.

Ammonium carbonate is prepared by subliming a mixture of crude ammonium sulfate with calcium carbonate. It is interesting to note that attempts to prepare same by aqueous crystallization have never met with success, hence attempts to restore effloresced ammonium carbonate by crystallization are futile.

Ammonium carbonate is a stimulant of particular value in diseases affecting the pulmonary mucous membrane, and hence it is used in pneumonia.

Dose.—300 mg. (5 grains).

SPIRITUS AMMONIÆ AROMATICUS—Aromatic Spirit of Ammonia (Sp. Ammon. Arom.)

Aromatic Spirit of Ammonia contains, in each 100 cc., not less than 1.7 Gm. and not more than 2.1 Gm. of total NH_3; and ammonium carbonate, corresponding to not less than 3.5 Gm. and not more than 4.5 Gm. as $(NH_4)_2CO_3$.

Storage.—Preserve in glass-stoppered bottles, in a cool place and protected from light.

Condensed Recipe.

Ingredients.—Translucent ammonium carbonate, 34 Gm.; ammonia water, 90 cc.; oils of lemon, lavender and nutmeg; alcohol, 700 cc.; distilled water enough to make 1000 cc.

Manipulation.—Dilute the ammonia water with 140 cc. of water, dissolve therein the carbonate and let stand for twelve hours. Dissolve the oils in the alcohol, then add the carbonate solution and enough water to make 1 liter. Let stand twenty-four hours and then filter. For details see U.S.P., p. 351.

Summarized Description.

Colorless when fresh, yellow when older; ammoniacal odor and taste; sp. gr., 0.900. For details see U.S.P., p. 351.

Remarks.—In making this preparation ammonia water is added to the official ammonium carbonate, and this means adding ammonia to bicarbonate and water to the carbamate; in other words, the solution of the official carbonate, in water containing ammonia. converts that mixed salt into the true carbonate, as shown above. This ammoniacal solution of the true carbonate is added to an alcoholic solution of the volatile oils of lemon, lavender flowers, and nutmeg. But the conversion of the bicarbonate and carbamate of the official salt into the true carbonate occurs completely only when the official salt is in "translucent pieces," as directed by the Pharmacopia. Translucent means intermediate between transparent and opaque. One cannot see through a translucent substance as one can through a pane of glass, but some light passes through the substance. Ground glass or thin pieces of horn are good examples of translucent substance. Examination of ammonium carbonate will show that it is difficult to keep it in translucent pieces, since the lumps become covered with white powder, which is wholly ammonium bicarbonate; that is, the carbonate gradually changes into the bicarbonate by the loss of ammonia and the absorption of moisture from the air. So eventually the entire mass of a sample of official carbonate will be converted into the bicarbonate, falling to a powder.

What happens when we try to use such effloresced carbonate—really bicarbonate—in the aromatic spirit? The ammonia water directed by the official process is only sufficient to convert the theoretic quantity of bicarbonate contained in the official salt into normal carbonate, while the balance of the bicarbonate, which would have been carbonate were the salt in translucent pieces, dissolves unchanged. So far, good! but the evil effect comes when we begin to add the aqueous solution to the alcoholic solution. The carbonate is soluble in alcohol, the bicarbonate is not, and if the aqueous solution contains any bicarbonate, the latter will be precipitated so soon as its solution is added to the alcoholic liquid.

Brown has shown that when the mixture of effloresced carbonate, water and ammonia water is allowed to stand the complete conversion to true ammonium carbonate occurs; hence the directions of U.S.P. XI to allow twelve hours of standing.

Aromatic spirit of ammonia, when freshly prepared, is colorless, but on standing it gradually becomes dark, eventually turning to an amber tint. This darkening has been ascribed to some chemical action between the oils which are used and the alkali. The pharmacist should prepare his customer for any change in the color of the two samples of this or any other preparation when a prescription for the same is repeated. In this special case it is better to dispense an aromatic spirit of ammonia which has aged sufficiently to be somewhat colored. At any rate, a pharmacist should never let a customer obtain a preparation of a color different from that of the first sample without calling the customer's attention to the difference in coloration and giving the reason for same.

Dose.—2 cc. (30 minims).

AMMONII CHLORIDUM—Ammonium Chloride

(Ammon. Chlorid.—Muriate of Ammonia)

NH_4Cl. Molecular weight, 53.50

Ammonium Chloride, when dried for twenty-four hours over sulfuric acid, contains not less than 99.5 per cent of NH_4Cl.

Summarized Description.

White, granular powder; cooling saline taste; somewhat hygroscopic; soluble in about 2.6 parts of water, in about 82 parts of alcohol and in about 10 parts of glycerin; volatilizes on heating. For details see U.S.P., p. 54.

For *tests for identity*, for *impurities* (heavy metals, thiocyanate, nonvolatile matter) and for *assay* see U.S.P., p. 55.

Remarks.—This salt is the oldest of the ammonium compounds, and in fact, the word ammonia was derived from its synonym, *sal ammoniac.* Legend tells us that this chemical was first prepared in the Libyan desert near the temple of Jupiter Ammon, and for this reason it was called sal ammoniac. Other investigators, however, claim that the sal ammoniac of Herodotus and Pliny was nothing but common salt, and that the first reference to ammonium chloride is found in writings of Geber (eighth century), in the Latin translations of which book it is called *sal armoniac.* Jastrow inclines to the opinion that the term came from "salt of Amanus" the latter being a mountain range in Northern Syria.

Ammonium chloride is made by subliming ammonium sulfate with common salt. According as the apparatus is arranged to collect the vapors in a dome or in a vessel at one side we obtain the ammonium chloride in the form of a cake or in a fine powder. (See Sublimation, p. 125.) Since sublimation is usually carried on in iron vessels, commercial ammonium chloride frequently contains traces of iron. These can be removed by treating the solution with ammonia water and granulating the filtrate. At present a large amount of ammonium chloride is made by subliming a crude chloride, obtained by passing illuminating gas (p. 501) through hydrochloric instead of sulfuric acid.

Commercial sal ammoniac is in the form of white, translucent, tough cakes, about 2 inches thick, convex on one side and concave on the other, being formed as a crust in the dome of the subliming apparatus. The official ammonium chloride is a white, crystalline powder, permanent in the air, and soluble in 3 parts of water, but only sparingly soluble in alcohol. This crystalline powder is obtained usually by granulation.

The ammonium chloride, as just mentioned above, is quite volatile, and its vapors cause red litmus paper to turn blue, and blue litmus paper to turn red. Such substances as convert both colors of litmus paper to the opposite colors are termed *amphoteric.* In the case of the sal ammoniac this phenomenon has been used as the basis of the claim that ammonium compounds are not definite compounds, but merely combinations of ammonia gas with the corresponding acid. Smith finds that between 280° and 330° C. not more than 67 per cent of the chloride is dissociated into NH_3 and HCl.

Ammonium chloride is a valuable stimulant and expectorant, and its vapor is frequently used as an inhalant in bronchial troubles, and numberless inhalers have been devised for its administration. In most cases their principle of action is the sucking into the nose or throat of air which has passed through hydrochloric acid and ammonia, and which is thus charged with ammonium chloride.

Noack reports that a mixture of ammonium chloride, sodium carbonate, and water is useful as an inexpensive chilling mixture, causing a temperature drop of 31° C.

Dose.—1 Gm. (15 grains).

AMMONII SALICYLAS—Ammonium Salicylate

(Ammon. Salicyl.)

$NH_4C_7H_5O_3$. Molecular weight, 155.08

Ammonium Salicylate, when dried for twenty-four hours over sulfuric acid, contains not less than 98 per cent of $C_6H_4.OH.COO.NH_4$.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless, lustrous, monoclinic prisms or white crystalline powder; saline and bitter, then sweetish taste: soluble in about 1 part of water and in about 2.5 parts of alcohol. For details see U.S.P., p. 55.

For *tests for identity* and for *impurities* (heavy metals) see U.S.P., p. 55.

Remarks.—This official, made by neutralizing ammonia water with salicylic acid and either crystallizing or granulating the solution by evaporation on water bath, is preferred by some physicians to sodium salicylate.

Dose.—1 Gm. (15 grains).

Ammonii Iodidum (U.S.P. IX; N.F. VI) or *Ammonium Iodide,* NH_4I, is made by treating ammonium sulfate with potassium iodide, as shown in the following equation:

$$(NH_4)_2SO_4 + 2KI = K_2SO_4 + 2NH_4I.$$

The resulting potassium sulfate is separated from the ammonium iodide by precipitation with alcohol. It might be well here to refer to the ingenuity exercised in attempts by the manufacturing chemist to remove the by-products from the chemical desired. It will be noticed that, whenever possible, the chemist arranges that the by-product be an insoluble salt when the product desired is soluble. This, for instance, is shown in the manufacture of the solution of potassa (p. 461). When the product desired is insoluble, then the manufacturer aims to make the by-product a soluble body. This is shown in the manufacture of calcium carbonate (p. 525).

In one case the soluble body is freed from the insoluble body by filtration; in the other case, the insoluble substance is freed from the soluble side-product by washing. But as the formation of an insoluble side-product is sometimes difficult, as was shown in the case of the manufacture of hydrobromic acid, recourse was had, in the Fothergill process, to the sparing solubility of potassium bitartrate, and into this salt was the potassium bromide converted by use of tartaric acid. In hydrobromic acid we have a product which can be separated from the side-product by distillation, and in the commercial process distillation is employed, but in the case of the ammonium iodide none of the schemes of separation just described is applicable, it being impracticable to form an insoluble or sublimable potassium salt, so recourse is had to the solubility of the ammonium iodide in alcohol and the comparative insolubility of potassium sulfate in the same liquid. Hence the aqueous solution of the two salts is concentrated, alcohol is added, and the mixture cooled, and after the potassium sulfate has separated, the hydro-alcoholic solution of ammonium iodide is filtered and rapidly granulated by evaporation on a water bath.

The iodide may also be made combining iodine and ammonia water in the presence of hydrogen dioxide as shown below,

$$2NH_3 + I_2 + H_2O_2 = 2NH_4I + O_2$$

This reaction should be conducted with the utmost caution, as the frightfully explosive nitrogen iodide, is apt to be formed when ammonia and iodine are brought together.

Ammonium iodide has the form of minute cubic crystals or white granular powder, very rapidly becoming yellowish or yellowish brown, due to the loss of ammonium and the separation of free iodine. So weak is the combination of the ammonium and the iodine that, during the process of evaporation, the iodine becomes liberated, and it is necessary to add ammonia water or, better, ammonium sulfide, from time to time. It is said that ammonium iodide can be preserved in its original white color by hanging down into the bottle from its neck a cheese-cloth bag containing a lump of ammonium carbonate.

Ammonium iodide is used as a resolvent. When dispensed for internal use, the pharmacist should be careful to see that the product is colorless, and if brown, to bleach with ammonium sulfide, as directed above.

Dose.—300 mg. (5 grains).

LABORATORY EXERCISES

MAKE AMMONIUM SULFATE

Ammonia water (10 per cent)	340 grains or ——	Gm.
Diluted sulfuric acid (10 per cent)	980 grains or ——	Gm.

Place the ammonia water in a pint evaporating dish, add the sulfuric acid gradually until faintly acid to litmus paper, using more than the amount given above if necessary.

Then add extra ammonia water, drop by drop, until alkaline to litmus paper. Place dish on wire gauze and evaporate to dryness.

Explanation.—This process gives us an illustration of a simple reaction, viz.: ammonia plus sulfuric acid gives ammonium sulfate.

Express this reaction by equation, writing the formula of each of the compounds mentioned above and the number of molecules of each substance entering the equation.

Calculations.—Next work out molecular weight of each of the above compounds (as shown in solution of soda), and through these molecular weights answer the following problems:

1. How many grams of ammonia gas and absolute sulfuric acid are needed to make 132 grains of ammonium sulfate?
2. How many grains of 10 per cent ammonia water and of 10 per cent sulfuric acid are needed to make 132 grains of ammonium sulfate?

Remarks on Process.—*Convert grains into grams* by dividing by 15.432.

Add the acid gradually to the ammonia, as the reaction is apt to be quite violent.

Litmus paper (see p. 395).

In testing with litmus paper dip a glass rod into the liquid and thus bring 1 drop of the liquid on the piece of litmus paper moistened with water. Never dip the litmus paper into the mixture.

Add acid until faintly acid—that is, it may chance that the theoretic quantities given above may not yield exact results, due to some variation in strength of either acid or alkali. In such case we therefore look for *results* rather than figures, and use an extra quantity of the ingredients to get the results, if necessary.

Thus, if after adding the directed quantity of acid, the mixture is still alkaline (until a drop turns red litmus blue), add acid until faintly acid (turns blue litmus red).

Usually, after the acid is added, the reaction will be distinctly acid, as the ammonia is more apt to lose strength on standing than is the acid. If such is the case, add ammonia until the mixture is distinctly alkaline—until a drop turns red litmus paper blue.

Be sure to have evaporating mixture alkaline. An excess of acid will spoil the product; an excess of alkali will have no hurtful result, since the excess of ammonia will be driven off as the salt reaches dryness.

Evaporate to dryness, but do not continue heat after dryness—as the ammonium sulfate is volatile.

MAKE AMMONIUM IODIDE

Potassium iodide	½ troy ounce or	—— Gm.
Ammonium sulfate	109 grains or	—— Gm.
Water	¼ fluidounce or	—— cc.

Put salts in Erlenmeyer flask, add the water while boiling, stir well, and let cool. Then add 1 drachm alcohol, cool the mixture with ice or running water, and throw the mixture on funnel plugged with cotton. When the liquid has filtered through, wash precipitate with 1 drachm of a mixture, consisting of alcohol, 1 part, water, 2 parts. Then put filtrate in pint evaporating dish, and evaporate solution rapidly to dryness, stirring constantly.

Explanation.—In this process a double decomposition occurs between the potassium iodide and ammonium sulfate, whereby potassium sulfate and ammonium iodide are formed.

Equation:

$$KI + (NH_4)_2SO_4.$$

Complete this equation.

Calculation.—Figure out molecular weights of each of the above substances, and from the molecular weights learn the weights by which the two chemicals combine. Then solve the following problems:

1. How much potassium iodide and ammonium sulfate are needed to make 290 grains of ammonium iodide?

2. How much potassium iodide and ammonium sulfate are needed to make 218 grains of ammonium iodide?

Compare these figures with above recipe, and see how closely they agree.

Remarks on Process.—Looking at the explanation of the chemistry of the process, we see that the products of the reaction between potassium iodide and ammonium sulfate are potassium sulfate and ammonium iodide. Now it chances that both of these chemicals, like the substances from which they are made, are soluble in water. How are we to obtain the ammonium iodide we desire free from the potassium sulfate?

In all manufacturing chemistry effort is made to get all the *reaction* products save the one we desire in some form different from the one we want.

Thus, in making solution of soda, we choose as the sodium ingredient sodium carbonate, knowing that that would produce with the lime insoluble calcium carbonate, thus leaving the soda itself in the solution, free from any other substance. Again, if we want an insoluble body, say, precipitated chalk, we try to get the other reaction products in a soluble form. (See p. 525.)

In the ammonium iodide we cannot think of any salt we can use that will obtain for us the second reaction product in insoluble form. Every combination we think of will yield some chemical soluble in water, even as is ammonium iodide. Therefore, we have to devise some way of separating the iodide from the potassium sulfate, and we accomplish this by use of alcohol, in which the iodide is freely soluble, while the sulfate dissolves but slightly.

Filter through funnel plugged with cotton. See granulated ferrous sulfate, p. 565.

Evaporate rapidly, as the product is quite unstable, easily giving up its iodide and becoming brown. For this reason, during evaporation, it is advisable to add a drop of ammonium sulfide test solution, from time to time, to prevent decomposition.

Ammonii Nitras (U.S.P. 1890) or *Ammonium Nitrate*, NH_4NO_3, **was first made by Glauber (1667) by treating nitric acid with spirit of hartshorn.**

It is now usually made by treating ammonium carbonate with nitric acid and crystallizing by evaporation of the solution. It occurs in colorless crystals, soluble in 5 parts of water, and like all ammonium compounds, is easily sublimed. It is interesting to note that when exposed to a current of dry ammonia gas its crystals absorb the gas and melt, yielding eventually a crystalline mass containing 25 per cent of ammonia.

Its chief use is in the production of *laughing gas*, N_2O, which is yielded by heating the salt in a retort.

It is interesting to note that if, instead of the nitrate, ammonium nitrite is heated, nitrogen is produced.

Let us put the equations side by side:

$$NH_4NO_3 + \text{heat} = 2H_2O + N_2O,$$
$$NH_4NO_2 + \text{heat} = 2H_2O + N_2.$$

Ammonii Valeras Acidus (N.F. VI) or *Ammonium Valerate*, which is supposedly $NH_4C_5H_9O_2$ but which is frequently of variable composition, is made by passing dry ammonia gas into monohydrated valerianic (or valeric) acid. In the manufacture of this product it is very important to secure the proper valerianic acid. As noted on p. 687, most of the commercial acid is that containing 3 molecules of water, and this acid will not yield a satisfactory ammonium salt.

Ammonium valerate occurs in snow-white, four-sided, tabular crystals, having the characteristic odor of valeric acid, and a sharp, sweetish taste. It is used as a sedative in hysteria. *Dose.*—125 mg. (2 grains).

Ammonium Sulfate $(NH_4)_2SO_4$.—Ammonium sulfate was recognized in the Pharmacopœia of 1880, and deserves merely passing notice. As already mentioned, it is made in large quantity from ammoniacal liquor of gas works, and is the commercial source of ammonia compounds. It can be made by combining ammonia water with sulfuric acid, as explained above.

When ammonium sulfate is electrolyzed under proper conditions, *ammonium persulfate* ($(NH_4)_2S_2O_8$) is formed. This is now largely used as an oxidizing reagent.

Ammonium Phosphate (N.F. V), $(NH_4)_2HPO_4$, was another official salt of the Pharmacopœia of 1880. It is made by treating phosphoric acid with ammonia water. A modification of this, the double salt of ammonium and sodium phosphate, NH_4NaHPO_4, is used in chemical work under the name *microsmic salt* or "*Phosphorsalz.*" This salt, when melted on the loop of platinum, forms a transparent bead, similar to the borax bead, and when various metallic salts are melted therein, it assumes characteristic colors.

Ammonii Hypophosphis (N.F. VI), or *Ammonium Hypophosphite*, $NH_4PH_2O_2$, is a constituent of syrup of ammonium hypophosphite, N.F. (See p. 223.) *Dose.*—200 mg. (3 grains).

Another unofficial ammonium compound largely used in chemical work is the so-called *ammonium sulfide*. This is more properly called ammonium sulfydrate as the reagent used in precipitation in chemical work usually has the composition NH_4HS. However, the composition of this reagent varies, some samples containing a large excess of sulfur, and containing such bodies as $(NH_4)_2S_4$, $(NH_4)_2S_5$, and $(NH_4)_2S_7$. This test solution is made by saturating ammonia water with hydrogen sulfide gas.

BIBLIOGRAPHY

Lithium.—(History) Vauquelin, Jl. de ph., 4, 1818, 174; Berger, Sch. Wsch. f. Ch. u. Ph., 250, 1912, 597; Dyson, Ph. Jl., 127, 1931, 202. (Sources) Anon., Jl. Frank. Inst., 190, 1920, 595; Anon., Jl. Soc. Ch. Ind., 45, 1926, 62; Bayley, C.A., 23, 1929, 1349; Schwartz, C. A., 25, 1931, 1186. (Isolation) Braun, C.A., 24, 1930, 560. (Density) Richards and Brink, Jl. Am. Ch. Soc., 29, 1907, 117. (Flame test) Stiles, U. S. Dept. Agr. Bull., No. 139, p. 108. (Production) Hauer, A.J.P., 29, 1857, 166. (Therapeutics) Spoto, C.A., 25, 1931, 1331.

Lithium Bromide.—(Manufacture) Yvon. Ph. Jl., [3], 6, 1875, 221.

Lithium Carbonate.—(Manufacture) Schieffelin and Cappon, Jl. Soc. Ch. Ind., 27, 1908, 549.

Ammonium.—(Structure) Smith, A.Ph.A., 56, 1908, 284; and 37, 1915, 38; Werner, A., 322, 1902, 276; Meyer and Lecco, A., 180, 1875, 173; McCoy and Moore, Jl. Am. Ch. Soc., 33, 1911, 273; Schlubach and Ballauf, C.A., 16, 1922, 693.

Ammonia.—(History) Trenmann, Ch. Zt., 33, 1909, 49. (Manufacture) Anon., Ph. Jl., 13, 1853, 29, 63 and 113. (Synthesis) Bernthsen, 8th Int. Congr. App. Ch., 28, 1912, 182; Hosmer, Jl. Ind. Eng. Ch., 9, 1917, 426; Tour, Jl. Ind. Eng. Ch., 12, 1920, 844; Claude, Pharm. Era, 53, 1920, 8; West, Jl. Soc. Ch. Ind., 40, 1921, 420R.; Bartell, Jl. Ind. Eng. Ch., 14, 1922, 516; Sadtler, A.J.P., 95, 1923, 278; Lheure, C.A.,

17, 1923, 1308; Larson and Brooks, Jl. Ind. Eng. Ch., 18, 1926, 1305; Adams, *ibid.*, 18, 1926, 1182; Ernst and Sherman, *ibid.*, 19, 1927, 196; Crane and Allen, *ibid.*, 20, 1928, 1128; Anon., Nat. Dr., 58, 1928, 117; Anon., Jl. Soc. Ch. Ind., 48, 1929, 591; Anon., Jl. and. Eng. Ch., 22, 1930, 433; Crane, *ibid.*, 22, 1930, 795; Berliner and Burke, C.A., 25, 1931, 777. (Tests) Nessler, Zt. analyt. Ch., 7, 1868, 415.

Ammonia Water.—(Density) Price and Hawkins, Jl. Soc. Ch. Ind., 43, 1924, 113T.

Ammonium Hydroxide.—(Structure) Tommasi, Comp. rend., 98, 1884, 812; Caven, Jl. Soc. Ch. Ind., 42, 1923, 164 and 744; Moore, *ibid.*, 42, 1923, 343.

Solution of Ammonium Acetate.—Pile, A.Ph.A., 14, 1866, 226.

Ammonium Bromide.—(Manufacture) Pile, A.Ph.A., 22, 1874, 434; Rice, A.J.P., 45, 1873, 249.

Ammonium Carbonate.—(Composition and efflorescence) Divers, Ch. News, 22, 1870, 73 and 85; Vogler, Zt. analyt. Ch., 17, 1878, 451; McIntyre, A.Ph.A., 23, 1875, 607; Fauerholt, C.A., 16, 1922, 2455; Self and Corfield, Ph. Jl., 116, 1926, 132; Cripps and Hoyland, *ibid.*, 121, 1928, 236 and 270.

Aromatic Spirit of Ammonia.—(History) James, Pharmacopœia Universalis, 1752, 475. (Chemistry) Brown, Proc. Ky. Ph. A., 35, 1912, 136; Tichborne, Ph. Jl., [2], 1, 1859, 16. (Uses) England, A.Ph.A., 49, 1901, 180.

Ammonium Chloride.—(History) Lippmann, Ch. Zt., 33, 1909, 117; Jastrow, Ann. Med. Hist., 1, 1917, 242; Ruska, Zt. angew. Ch., 41, 1928, 1321. (Manufacture) Dubosc and Heuzy, Am. Dr., 19, 1890, 168. (Freezing mixture) Noack, Jl. Ind. Eng. Ch., 21, 1929, 1001.

Ammonium Iodide.—(Manufacture) Babcock, A.Ph.A., 14, 1866, 245; Brocksmit, Pharm. Weekbl., 54, 1917, 1373.

Ammonium Nitrate.—Lloyd, Am. Dr., 16, 1887, 101.

Ammonium Valerate.—(Manufacture) Procter, A.J P., 29, 1857, 27; Crew, A.J.P., 32, 1860, 109; Hager, A.Ph.A., 28, 1880, 134.

Ammonium Sulfide.—(Composition) Bloxam, Jl. Ch. Soc., 67, 1895, 277.

Ammonium Sulfate.—Parrish, Jl. Soc. Ch. Ind., 45, 1926, 494.

Ammonium Persulfate.—Essen and Krilov, C.A., 21, 1927, 1935.

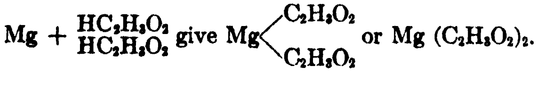
CHAPTER XXVIII

THE ALKALINE EARTH METALS

THE four elements, magnesium, calcium, strontium, and barium, are called alkaline earth metals because their oxides, MgO, CaO, SrO, and BaO, were called alkaline earths by early investigators—alkaline, because they turned red litmus blue, as do the alkalis, and earths, because differing from the alkalis in being found abundantly on the crust of the earth.

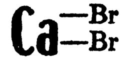
In passing from the alkalis—lithium, sodium, potassium, and ammonium—to the alkaline earths—magnesium, calcium, strontium, and barium—we not only pass into a new analytic groups of metals, but also a group the valence of which is different.

The alkalis exhibit the valence I; that is, 1 atom of an alkali metal replaces 1 atom hydrogen in an acid, or in combining directly with a negative element, takes up but one of the free bonds of that element. The alkaline earths are bivalent—can replace 2 atoms of hydrogen in an acid. Thus, studying the formula of magnesium acetate, since 1 molecule of acetic acid, $HC_2H_3O_2$, contains only 1 atom of replaceable hydrogen, 2 molecules of the acid will be required to furnish the 2 atoms of hydrogen demanded by 1 atom of magnesium, and the union will be as follows:



$$Mg + \begin{matrix} HC_2H_3O_2 \\ HC_2H_3O_2 \end{matrix} \text{ give } Mg\begin{matrix} \diagup C_2H_3O_2 \\ \diagdown C_2H_3O_2 \end{matrix} \text{ or } Mg\ (C_2H_3O_2)_2.$$

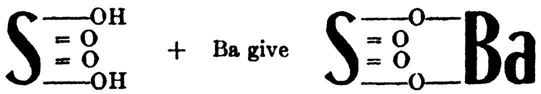
Again, bromine, having the valence I, and calcium, the valence II, unite as follows:



$$Ca\begin{matrix}-Br\\-Br\end{matrix}$$

$CaBr_2$.

while sulfuric acid, H_2SO_4, with two replaceable hydrogen atoms, combines with barium like this:



(H_2SO_4) (BaSO₄)

MAGNESIUM

Symbol, Mg. Atomic weight, approximately 24

In the beginning of the eighteenth century a secret remedy was introduced under the name of "magnesia alba," thus differentiating it from the already popular *magnesia nigra*, which is now known as the ore *pyrolusite* or manganese dioxide (p. 540). A recipe for this magnesia alba was published by Valentinus, of Giessen, in 1707, who obtained it by evaporation of the mother liquor from saltpetre, and lixiviation of the calcined residue.

Before this, magnesium sulfate was described by Nehemiah Grew, having been obtained by him by evaporation of the water of the Epsom spring.

Neither of these writers touched upon the composition of the two compounds, magnesium oxide and magnesium sulfate, and the chemical history of magnesium really begins with the investigation of Black (1755), who proved that magnesium carbonate or magnesite was different from calcium carbonate or limestone. The metal was first isolated by Sir Humphry Davy in 1808, during his classic researches in electrolysis. Davy obtained the metal in impure form, the first pure metal being isolated in 1830 by Bussy, by the action of metallic potassium upon magnesium chloride. In 1856 St. Clair Deville devised the chemical method for the isolation given below.

The chief ores of magnesium are *magnesite*, just mentioned (magnesium carbonate); *dolomite*, a mixed carbonate of magnesium and calcium; *carnallite*, a mixture of potassium and magnesium chloride. (See p. 458.) Aside from these ores, from which the magnesium compounds used in pharmacy are generally derived, there are several magnesium minerals which are of interest other than pharmaceutic. Thus *serpentine*, a green stone, much used in building, is magnesium silicate, as is also *talcum* (*French chalk*), and *meerschaum*, well known as the substance of which the best pipes are made; *asbestos* is a mixed silicate of magnesium and calcium.

The chemical method of isolation of magnesium mentioned above is by heating magnesium chloride with metallic sodium, sodium chloride and calcium fluoride being added to the reacting mixture as a *flux*—that is, as an agent to remove contaminations in the form of a fusible mass. It is now made by the electrolysis of molten magnesium chloride in a bath of sodium chloride and calcium fluoride.

Magnesium is a light, silvery-gray metal, with the specific gravity of 1.75, and usually enters commerce in the form of rods or of thin ribbons. While affected by the air, it does not react with the same as violently as do the alkaline metals. Hence it is unnecessary to keep it under petroleum, as was the case with sodium and potassium. When magnesium is brought into contact with a flame, it burns with a brilliant white light, with the formation of magnesium oxide. This property is made use of in the magnesium lantern for theatrical purposes, in which case the magnesium, in the form of ribbons, is allowed to burn at the point of contact of an oxyhydrogen flame. *Flashlight* consists of magnesium in finely powdered form, mixed with powdered potassium chlorate. This mixture, when blown into a flame, ignites instantaneously, producing a brilliant illumination, and is, therefore, largely used for photographic purposes. (See p. 531.) It should be borne in mind that flashlight is a substance by no means free from danger, and, in fact, should be handled with considerable caution. Several fatal accidents, due to the careless handling of flashlight, are on record.

Among the tests for magnesium are: flocculent precipitate of magnesium hydroxide, produced when potassium hydroxide is added to a solution of a magnesium salt, and the white precipitate of magnesium carbonate, produced when the soluble carbonate is added to the solution of magnesium salt. The most characteristic test, however, is the granular precipitate of magnesium ammonium phosphate, produced when a solution of sodium phosphate and ammonia water is added to a solution of magnesium salt. In the manufacture of the salts of magnesium the carbonate is usually employed as a magnesium compound. The following compounds of magnesium and their preparations are official:

Magnesium oxide, 96 per cent absolute MgO.
Heavy magnesium oxide, 96 per cent absolute MgO.
Magma of magnesia, 7 to 8.5 per cent absolute $Mg(OH)_2$.
Magnesium carbonate, approximately $(MgCO_3)_4Mg(OH)_2.5H_2O$, should contain 39.2 to 41.5 per cent MgO.
Solution of magnesium citrate. A pharmaceutical.
Magnesium sulfate, 99.5 per cent absolute $MgSO_4.7H_2O$.

MAGNESII OXIDUM—Magnesium Oxide

(Mag. Oxid.—Magnesia, Light Magnesia)

MgO. Molecular weight, 40.32

Magnesium Oxide contains, after ignition, not less than 96 per cent of MgO. Its loss in weight, during ignition, does not exceed 10 per cent.

Storage.—Preserve in well-closed, moisture-proof containers.

Summarized Description.

White, very bulky, very fine powder; earthy but not saline taste; absorbs water and carbon dioxide from the air; almost insoluble in water; insoluble in alcohol; soluble in diluted acids. For details, see U.S.P., p. 225.

For *tests for identity*, for *impurities* (foreign soluble salts, excess of water of hydration, carbonate, excess of calcium, iron, heavy metals, arsenic), and for *assay*, see U.S.P., p. 225.

MAGNESII OXIDUM PONDEROSUM—Heavy Magnesium Oxide

(Mag. Oxid. Pond.—Heavy Magnesia)

Heavy Magnesium Oxide contains, after ignition, not less than 96 per cent of MgO. Its loss in weight, during ignition, does not exceed 10 per cent.

Storage.—Preserve in well-closed, moisture-proof containers.

Summarized Description.

White, dense, very fine powder. For details, see U.S.P., p. 226.

Sedimentation tests for water-absorbing capacity are provided for both the light and the heavy oxides by U.S.P., XI.

For *tests for identity*, for *impurities* and for *assay*, see magnesium oxide.

Remarks.—These two magnesias are prepared by the calcination of light and heavy magnesium carbonates respectively, and the carbonate can be made light or heavy as precipitated from cold dilute solutions or from hot concentrated solutions, as already explained in discussion of the formation of light and heavy precipitates (p. 167). Bear in mind that *magnesia is not magnesium.* Magnesium is the metal—the element; magnesia is the oxide of the metal, MgO, not the hydroxide, as was the case with soda and potassa.

The medicinal use of light and heavy magnesia is identical, both being laxative and antacid, the advantage of the heavy magnesia over the light magnesia depending entirely upon its greater density, the average heavy magnesia occupying only about one quarter the bulk of the light magnesia. This should be remembered in considering the dosage of the two preparations, they being generally employed in domestic practice, and then given by measure rather than by weight. A dessertspoonful of light magnesia is generally given as the dose, while of the heavy magnesia, a half teaspoonful to a teaspoonful is usually sufficient. In each case the customer should be directed to administer the substance in a moist condition. Thus, in giving the heavy magnesia, place from 1 to 2 teaspoonfuls of water in a tablespoon, and add thereto the teaspoonful of magnesia. The process should never be reversed, as the adding of water to the magnesia gives rise to hard lumps, whereas by the method just given a smooth mixture is obtained.

Under no circumstance should the pharmacist advise placing dry magnesia in the mouth, as the chemical will then adhere to the tongue and roof of the mouth, producing so disagreeable an impression that the victim will always unpleasantly remember the person giving such advice.

The addition of water to magnesia produces magnesium hydroxide by the following reaction:

$$MgO + H_2O = MgO_2H_2 \text{ or } Mg(OH)_2.$$

Dose of both oxides of magnesium, as given by the Pharmacopœia: antacid, 250 mg. (4 grains); laxative, 3 Gm. (45 grains).

MAGMA MAGNESIÆ—Magnesia Magma

(Magma Mag.—Milk of Magnesia)

Magnesia Magma is an aqueous suspension of magnesium hydroxide containing not less than 7 per cent and not more than 8.5 per cent of $Mg(OH)_2$. For purposes of mimimizing the action of the glass container on magnesia magma, 0.1 per cent of citric acid may be added.

Note.—One-half cc. of a volatile oil or a blend of volatile oils, suitable for flavoring purposes may be added to each 1000 cc. of magnesia magma.

Storage.—It is recommended that magnesia magma be stored at temperatures not exceeding 35° C. It should not be permitted to freeze.

Condensed Recipe.

Add an aqueous solution of sodium hydroxide (100 Gm. to 1000 cc.) to a boiling solution of magnesium sulfate (300 Gm. to 650 cc.) continuing the boiling for thirty minutes. Then wash magma with water by decantation until free from sulfates and concentrate mixture by evaporation to 7 per cent strength. For details, see U.S.P. X.

Summarized Description.

Thick, white, liquid mixture; alkaline reaction. For details, see U.S.P., p. 223.

For *tests for identity,* for *impurities* (soluble alkalis, soluble salts, carbonate, calcium, arsenic) and for *assay,* see U.S.P., p. 223.

Remarks.—This *milk of magnesia* is usually made by precipitation. The recipe of U.S.P. IX directed trituration of a paste of magnesium carbonate and water with a solution of sodium hydroxide, a method distinctly inferior to that of the U.S.P. X. No recipe is given in U.S.P. XI, which however gives permission for addition of volatile oils for flavoring purposes. Magma of magnesia is a very popular antacid and laxative.

Dose.—Antacid, 4 cc. (1 fluidrachm); Laxative, 15 cc. (4 fluidrachms).

MAGNESII CARBONAS—Magnesium Carbonate

(Mag. Carb.—Carbonate of Magnesia)

Magnesium Carbonate is a basic hydrated magnesium carbonate, equivalent to not less than 39.2 per cent and not more than 41.5 per cent of MgO.

Summarized Description.

Light, white, friable masses or bulky white powder; slight earthy taste; permanent in air; practically insoluble in water, which is however made alkaline; insoluble in alcohol; soluble in diluted acids, with effervescence; is calcined by strong heat. For details, see U.S.P., p. 224.

For *tests for identity*, for *impurities* (foreign soluble salts, excess of calcium, iron, arsenic, heavy metals) and for *assay*, see U.S.P., p. 224.

Remarks.—It will be noticed that this chemical is one of the three official carbonates not possessing the formula of the true carbonate. (See p. 505.) In all these cases the deviation from the theoretic is not intentional, but is due simply to the fact that the true carbonates are unstable, and the formula given represents, as nearly as possible, the composition of the purest form which this chemical ordinarily assumes.

Magnesium carbonate is made by the double decomposition of magnesium sulfate with sodium carbonate.

According to conditions of chemical action—temperature and concentration of reacting solutions, treatment after formation, etc.—the finished product can have most varying composition.

Thus, under differing conditions, from solutions of magnesium sulfate and sodium carbonate may be obtained $MgCO_35H_2O$; $MgCO_32H_2O$; $(MgCO_3)_2Mg(OH)_22H_2O$; $(MgCO_3)_3Mg(OH)_25H_2O$; and $(MgCO_3)_3Mg(OH)_2$, combined with 5 to 11 molecules of water respectively.

The usual commercial carbonate has the composition $(MgCO_3)_4Mg(OH)_25H_2O$, and this formula was assigned to it by U.S.P. VIII. The present Pharmacopœia gives no formula, merely stating that it must represent 39.2 per cent of magnesium oxide.

As mentioned above, according as the precipitation takes place in a cold diluted solution or in hot concentrated solutions, do we obtain light precipitated carbonate or heavy precipitated carbonate. As far as the carbonate itself is concerned, this is of little importance, but when we consider that the two official forms of magnesia are derived from the light and heavy carbonates respectively, then the question forces itself upon our notice.

The official magnesium carbonate is a light form, the heavy carbonate being of interest merely in the formation of heavy magnesia, and for this purpose manufacturers resort to extraordinary pains to manufacture a dense magnesium carbonate.

Much magnesium carbonate is marketed in cubes wrapped in blue paper. As the carbonate readily adsorbs odors it should be kept in closed containers.

Magnesium carbonate is a valuable antacid and a laxative. The technical carbonate is used on a large scale as a heat insulator.

Dose.—Antacid, 600 mg. (10 grains); Laxative, 8 Gm. (2 drachms).

LIQUOR MAGNESII CITRATIS—Solution of Magnesium Citrate (Liq. Mag. Cit.)

Solution of Magnesium Citrate contains, in each 100 cc., an amount of magnesium citrate corresponding to not less than 1.6 Gm. and not more than 1.9 Gm. of MgO.

Condensed Recipe.

Ingredients.—Magnesium carbonate, 15 Gm.; citric acid, 33 Gm.; syrup, 60 cc.; potassium bicarbonate, 2.5 Gm.; distilled water, enough to make 350 cc. Oil of lemon as flavor; purified talc, as clarifier.

Manipulation.—Dissolve the acid in 150 cc. of hot water and mix with a paste of magnesium carbonate in 100 cc. of water. When solution is effected, add the syrup, heat to boiling, add the oil of lemon triturated with the talcum, filter while hot into an appropriate bottle (previously scalded with boiling water), add boiled water enough to make 350 cc., then the potassium bicarbonate, and quickly stopper the bottle. Permission is given to use sodium bicarbonate instead of the potassium salt. For details, see U.S.P., p. 214.

Summarized Description.

Slightly yellow, clear, effervescent liquid; pleasant acidulous taste.

For *tests for identity*, for *impurities* (tartaric acid, sulfate, chloride) and for *assay*, see U.S.P., p. 215.

Remarks.—This official solution is made by treating the carbonate with citric acid, sweetening with syrup and flavoring with oil of lemon, and bottling with an excess of carbon dioxide formed by addition of potassium bicarbonate. The finished product, dispensed in stout bottles securely stoppered with cork and wire or with a metallic cup, is popular under the name of *purgative lemonade.*

This recipe has been criticized because the product does not keep. On standing a few weeks there form within the tightly corked bottle stringy masses, which not only spoil the appearance, but also destroy the pleasant taste. These masses are none other than microscopic plants, produced by spores introduced into the bottle before filling, and thriving in the weak saccharine solution. The formation of these plants can be prevented by the simple precaution of sterilization. If care be taken to scald the bottles before putting in the solution, immersing corks or caps in boiled water before being used, and using only freshly boiled water in preparing the solution and filtering through white paper, *not* the common gray, a product is obtained which, in the writer's experience, has kept perfectly for several months.

Occasionally, even with these precautions, a precipitation occurs in the bottled solution. In such cases, however, the precipitate is dense rather than stringy and is said to be due to the formation of normal citrate containing 13 molecules of water of hydration ($Mg_3C_6H_5O_7 + 13H_2O$). It is also said that if the ratio between the citric acid and the magnesium carbonate used in the recipe is 25 to 10 (about that of the official recipe) the precipitation is prevented.

As much of the citrate of magnesia solution on the market contains less citric acid than directed in the official recipe, U.S.P. XI provides a test for minimum limit of citric acid.

Dose.—350 cc. (12 fluidounces).

Effervescent magnesium citrate (U.S.P. 1890) is prepared by treating magnesium carbonate with citric acid and with sufficient water to produce the chemical action. The resulting pasty mass is then dried, preferably on a radiator, and then reduced to a powder and mixed with sodium bicarbonate, more citric acid, and sugar. This mixture is then moistened with strong alcohol, and granulated by passing through a coarse sieve, as described on p. 327. The official product must be put in warm, completely dried bottles, which should be sufficiently tightly sealed to prevent access of air.

The effervescent citrate is a very agreeable preparation, for when it is added to water, a refreshing effervescent draught is readily obtained. It is usually administered in tablespoonful doses.

MAGNESII SULFAS—Magnesium Sulfate

(Mag. Sulf.—Epsom Salt)

$MgSO_4.7H_2O$. Molecular weight, 246.49

Magnesium Sulfate, when rendered anhydrous by ignition, contains not less than 99.5 per cent of $MgSO_4$. It contains not less than 45 per cent and not more than 52 per cent of water.

Storage.—Preserve in air-tight containers.

Summarized Description.

Small, colorless, prismatic needles or rhombic prisms, cooling, saline, bitter taste; efflorescent; soluble in 0.8 part of water and in about 1.3 parts of glycerin; almost insoluble in alcohol. For details, see U.S.P.. p. 226.

For *tests for identity*, for *impurities* (chloride, heavy metals, arsenic) and for *assay*, see U.S.P., p. 226.

Remarks.—In magnesium sulfate—the well-known *Epsom salt*—we have the sulfate of a metal with the valence II.

Taking sulfuric acid, H_2SO_4, as the type, we find that, in each of the sulfates hitherto considered, the 2 hydrogen atoms in the acid were replaced by 2 atoms of the metal, since the 4 alkaline metals are univalent. On the other hand, the 4 alkaline earth metals, which we are now studying, have the valence II; that is, 1 atom of these metals can replace 2 atoms of hydrogen in an acid. The difference in these 2 groups of metals is best shown in a comparison of their sulfates, as here given.

Sulfates of the alkali metals:

K_2SO_4	Na_2SO_4	Li_2SO_4	$(NH_4)_2SO_4$
Potassium sulfate.	Sodium sulfate.	Lithium sulfate.	Ammonium sulfate.

Sulfates of alkaline earth metals:

$MgSO_4$	$CaSO_4$	$SrSO_4$	$BaSO_4$
Magnesium sulfate.	Calcium sulfate.	Strontium sulfate.	Barium sulfate.

As above mentioned, magnesium sulfate contains 7 molecules of water of crystallization. Of these, 6 molecules are lost by heating the crystals to 110° C., while the seventh molecule requires a heat of at least 200° C. to drive it off. This leads some to consider the linkage between the seventh molecule of water and the rest of the compound as stronger than is the case with the other six, and it has given rise to a supposed distinction in water of crystallization, the comparatively easily removed water being called water of crystallization, while the molecule of water tenaciously holding to the molecule being called water of constitution. This phraseology has however become obsolete.

Magnesium sulfate is made on an enormous scale commercially from the native magnesium minerals, dolomite or magnesite being generally employed. In the case of the first, the dolomite is calcined, whereby we obtain a mixture of the oxides of calcium, magnesium, and iron. The calcined mass is then treated with hydrochloric acid producing the chlorides of the three metals. The filtered solution is then evaporated, and during this process the magnesium chloride dissociates, as shown in the following equation:

$$MgCl_2 + O = MgO + Cl_2$$
$$\text{or } MgCl_2 + H_2O = MgO + 2HCl.$$

Hence the evaporated mass is a mixture of the chlorides of calcium and of iron, while the magnesium has been converted into sparingly soluble magnesium oxide. The two chlorides just mentioned are readily removed from the magnesium by treatment with water, and the magnesia residue thus freed from the iron and calcium is then treated with sulfuric acid, and the resulting sulfate purified by crystallization. In view of the peculiarity just mentioned regarding the instability of magnesium chloride, it might be here stated that the one way of obtaining a dry magnesium chloride is by the evaporation of a mixed solution of magnesium and ammonium chloride.

Magnesium sulfate is now largely produced as a by-product in the Dow process of obtaining bromine (p. 425).

Magnesium sulfate is a valuable saline cathartic and is a constituent of many of the most popular purgative waters. The chief objection to its use is the disagreeably bitter taste which the salt possesses, and it might here be stated that this disagreeable taste can be much lessened by administering the solution in an ice-cold condition.

Magnesium sulfate is also administered hypodermically in chorea.

Several fatal accidents have occurred from the substitution of zinc sulfate for magnesium sulfate, because of their identical crystalline form.

Dose.—15 Gm. (4 drachms).

Magnesii Sulfas Effervescens (U.S.P. VIII) is now recognized in the National Formulary under the name, *Sal magnesii sulfatis effervescens* (p. 327).

Liquor Magnesii Sulfatis Effervescens (N.F. IV) is an effervescent draught containing 25 Gm. of Epsom salt to the dose of 350 cc. Like solution of magnesium citrate, it is to be dispensed in strong bottles.

Sal Kissingense Factitium (N.F.), or *Artificial Kissingen Salt,* is a mixture of magnesium sulfate, sodium and potassium chlorides and sodium bicarbonate.

Sal Kissingense Factitium Effervescens (N.F.). (See p. 327.)

Sal Vichyanum Factitium (N.F.), or *Artificial Vichy Salt,* is a mixture of magnesium sulfate, sodium chloride and bicarbonate and potassium carbonate.

Sal Vichyanum Factitium Effervescens (N.F.). (See p. 327.)

TALCUM PURIFICATUM—Purified Talc

(Talc. Purif.)

Purified Talc is a purified, native, hydrous magnesium silicate, sometimes containing a small proportion of aluminum silicate.

Summarized Description.

Very fine, white or grayish-white powder; slippery to touch; odorless and tasteless; insoluble in water. For details see U.S.P., p. 380.

For *tests for identity,* for *impurities* (soluble substances, iron, carbonate) see U.S.P., p. 380.

Remarks.—This is talc, a mineral mined in New York, Virginia, and Italy, purified by treatment with hydrochloric acid. It is used as a filtering medium in those cases where precipitated calcium phosphate was directed by the Pharmacopœia of 1890, such as in making aromatic waters and some of the syrups. As a successful filtering agent it must not be finer than the 100 mesh directed by the former Pharmacopœia. Most talcum is intended for dusting purposes and is in a much finer state of subdivision.

Soapstone and *French chalk* are varieties of talc.

Magnesii Sulfis (U.S.P. 1890). This former official is made by passing sulfurous acid gas through milk of magnesia (magnesium hydroxide), as shown in the following equation:

$$Mg(OH)_2 + SO_2 = MgSO_3 + H_2O.$$

Magnesium sulfite is used as an antiferment, and given in doses of from 1 to 2 Gm.

CALCIUM

Symbol, Ca. Atomic weight, approximately 40

This element occurs as carbonate in the well-known minerals, *limestone, chalk*, and *marble*. *Gypsum* (or in the exsiccated form, commercial *plaster of paris*) is calcium sulfate, and the same substance in crystalline form constitutes the beautiful mineral, *alabaster*. *Fluorspar*, the transparent crystals used so much in optics, is a form of calcium fluoride.

The word calcium is derived from the Latin word *calx*, lime, which has been in use since ancient days, its manufacture from mussel-shells being described by Dioscorides, while the caustic effect of burnt lime is mentioned by Pliny. Berzelius and Pontin (1808) obtained calcium amalgam by electrolysis of lime in the presence of mercury, and Davy, in the same year, obtained the free metal in impure form by distilling the mercury from the amalgam.

The metal is now obtained by treating calcium chloride with metallic sodium and zinc, the zinc aiding the sodium in removing the chlorine from the calcium chloride. It is also made by electrolysis of molten calcium chloride.

Calcium is silver-white, ductile, malleable, quite stable in the air, but burning with a brilliant yellowish flame. In the so-called *calcium light*, lime or calcium oxide is employed, this substance burning with a brilliant white light when introduced into an oxyhydrogen flame.

Among the tests for calcium is the precipitate of calcium carbonate, produced when a soluble calcium salt is treated with a solution of an alkaline carbonate. More characteristic, however, is the white precipitate of calcium oxalate, produced in solutions of calcium salts on addition of ammonium oxalate solution. Turning to oxalic acid (p. 671), it will be found that lime is its antidote by reason of this very reaction, calcium compounds converting oxalic acid into the insoluble and harmless calcium oxalate.

In making most of the calcium compounds, the precipitated carbonate is employed.

The Pharmacopœia recognizes the following compounds of calcium and their preparations:

Calcium hydroxide. At least 95 per cent absolute $Ca(OH)_2$.
Solution of calcium hydroxide. At least $^{14}/_{100}$ of 1 per cent absolute $Ca(OH)_2$.
Calcium bromide. From 84 to 94 per cent absolute $CaBr_2$.
Prepared chalk. Elutriated chalk containing at least 97 per cent $CaCO_3$.
Compound chalk powder, containing 30 per cent prepared chalk.
Chalk mixture, containing 6 per cent prepared chalk.
Precipitated calcium carbonate. At least 98 per cent absolute $CaCO_3$.
Calcium chloride. From 75 to 85 per cent $CaCl_2$.
Calcium lactate. At least 98 per cent $Ca(C_3H_5O_3)_2.5H_2O$.

To which might be added:

Chlorinated lime (considered among the chlorine compounds).
Calcium iodobehenate (considered among the oils).
Calcium gluconate (considered among the carbohydrates).
Calcium creosotate (see p. 793).

CALCII HYDROXIDUM—Calcium Hydroxide

(Calc. Hydrox.—Slaked Lime, Calcium Hydrate)

$Ca(OH)_2$. Molecular weight, 74.10

Calcium Hydroxide contains not less than 95 per cent of $Ca(OH)_2$.
***Storage.*—Preserve in air-tight containers.**

Summarized Description.

Soft, white, crystalline powder; alkaline slightly bitter taste; soluble in 630 parts of water at 25° C. and in 1300 parts of boiling water; also soluble in glycerin and in syrup; insoluble in alcohol. For details, see U.S.P., p. 100.

For *tests for identity*, for *impurities* (carbonate, HCl-insoluble matter and magnesium) and for *assay*, see U.S.P., p. 100.

Remarks.—This new official is merely a modification of the time-honored calx (or lime) of the previous Pharmacopœias. During recent years commercial medicinal lime has been slowly replaced by special brands of *slaked lime* or *calcium hydroxide* and the pharmacopœial committee now recognizes this fact by directing for the manufacture of lime-water the carefully prepared hydroxide and by preparing more elaborate tests for purity. The oxide of U.S.P. X has been transferred to the National Formulary and is described below:

Calx (U.S.P. X; N.F. VI), or *Lime* represents the commercial calcium oxide, CaO, obtained by the calcination of limestone (p. 97).

When lime is treated with a small quantity of water, considerable heat (up to 150° C.) is evolved, and the lump falls to a fine white powder. This is due to the formation of calcium hydrate by the chemical reaction between the water and the lime, which is expressed by the following equation:

$$CaO + H_2O = Ca(OH)_2.$$

Some investigators think more water combines with the lime than is shown in the foregoing equation, Kosmann believing that the finished product of hydration is $Ca(OH)_2 7H_2O$.

The process is familiar under the name of *slaking lime*, the oxide being called *unslaked lime*, while the hydrate is slaked. In slaking small quantities of lime sometimes required in laboratory work, the heat is generated only in small quantities, so that at first glance it appears that no reaction is going on. The writer recalls one experience, when he rejected a sample of lime because of the difficulty of slaking, but found that, when he had thrown the same into water, a very energetic action would take place if a sufficient quantity was employed. This is particularly noticed in the slaking of small quantities required in small chemical operations and the writer's advice is for the operator to be guided by the eventual crumbling of the lump, instead of expecting an evolution of considerable heat.

Lime is used medicinally internally, when properly diluted with water, as an antacid. (See Lime Water.) When large quantities are applied, especially in the unslaked form, it acts as an escharotic and as a depilatory.

The use of lime in forming mortar in cements is so well know that the fact is here mentioned merely to call attention to that particular form called *Portland cement*. This is made either by calcining native cement rock or by mixing intimately finely powdered lime stone and clay and then calcining the mixture. It is of value because, when immersed in water, it forms a hard mass resisting the action of water, due to the formation of calcium silicate. For masonry constructions under water it is invaluable.

LIQUOR CALCII HYDROXIDI—Solution of Calcium Hydroxide

(Liq. Calc. Hydrox.—Liquor Calcis, Lime Water)

Solution of Calcium Hydroxide is an aqueous solution, containing in each 100 cc., at 25° C., not less than 0.14 Gm. of $Ca(OH)_2$. The content of calcium hydroxide varies with the temperature at which the solution is stored, being about 0.17 Gm. per 100 cc. at 15° C., and less at higher temperature.

Storage.—Preserve in well-filled, tightly stoppered bottles, in a cool place.

Condensed Recipe.

Add 3 Gm. calcium hydroxide to 1000 cc. of cool distilled water; shake frequently during one hour. Then let stand and decant the clear supernatant liquid. For details, see U.S.P., p. 205.

Summarized Description.

Clear, colorless liquid; alkaline in taste and in reaction; absorbs carbon dioxide from the air; becomes turbid on heating, but clears up on cooling. For details see U.S.P., p. 205.

For *tests for identity*, for *impurities* (alkalis and alkaline carbonates) and for *assay*, see U S.P., p. 205.

Remarks.—This official is largely sold under the name of *lime water*, and contains about 1/7 of 1 per cent of calcium hydroxide. It represents a saturated solution of calcium hydroxide in water, and emphasis should be laid on the fact that this is a case where a saturated solution is not necessarily a highly concentrated one. Another interesting point in connection with lime water is that the calcium hydroxide is more soluble in cold water than it is in hot water; and if a saturated solution prepared with cold water be warmed, it becomes turbid by the precipitation of the excess of lime.

Lime water is a preparation that is made by nearly all druggists, and that, unfortunately, in a careless way. Pharmacopœial lime water is *not* made by throwing a lump of lime into a crock, pouring water on it, and using the same lime for many subsequent crockfuls of water. In preparing lime water the pharmacopœial process should be used, and when once practiced, it will be found to be of little less inconvenience than the crude method above described, and a highly superior product is obtained.

The former Pharmacopœia directs that the liquid containing the undissolved lime in suspension be transferred to a glass bottle, and that this undissolved lime shall remain in the lime water until dispensed, in order that the solution be kept saturated. In dispensing, the clear fluid is to be decanted from the sediment. In practice, this part of the pharmacopœial requirement is rarely followed, and that in the interest of elegant pharmacy, as such procedure is almost sure to yield a more or less cloudy liquid, while most careful pharmacists desire to furnish a lime water which is as clear as crystal. In the writer's experience, ½-gallon bottles containing the water with an excess of undissolved lime were kept on hand securely corked, and when the ½-gallon dispensing bottle became empty, one of those kept in reserve was filtered, and a perfectly transparent liquid was obtained. The pharmacopœial objection to the use of filter paper is based on the fact that the fibers of the filter adsorb a certain quantity of calcium hydroxide, and, therefore, the first portion passing through the filter is deficient in lime strength. This disadvantage can be easily obviated by throwing away the first ounce or two of the filtered lime water and collecting the remainder in an appropriate container.

Several types of lime water containers have been devised. Most of these consist of a large bottle with syphon arrangement similar to that shown on p. 415, but fitted with a tight cork provided with two holes, through one of which passes the syphon tube and through the other a tube for entrance of air. This tube is connected with a wash bottle containing solution of alkali to absorb the carbon dioxide of the air. In preparing these the use of red rubber tubing should be avoided, as it contains sulfides which react with the alkaline calcium hydroxide to form calcium sulfide, frequently producing incompatibilities in the prescription in which the lime water is employed.

Solution of lime is a valuable antacid.

Dose.—15 cc. (4 fluidrachms).

Syrupus Calcis (U.S.P. VIII) or *Syrup of Lime* is described at length below. It is made by boiling together lime, sugar, and water. It has been used as an antacid and also as an antidote in oxalic acid poisoning. *Dose.*—2 cc. (30 minims).

LABORATORY EXERCISE

MAKE SYRUP OF LIME (U.S.P. VIII)

Recipe.—	Lime	6.5 Gm.
	Sugar	35.0 Gm.
	Water, a sufficient quantity,	
	To make	100.0 cc.

Slake the lime by the addition of 4 cc. of water with the aid of heat, then mix it and the sugar thoroughly in a mortar, so as to form a homogeneous powder; add the mixture to 50 cc. of boiling water, contained in a bright copper or tinned-iron vessel, and boil for five minutes, constantly stirring. Dilute the liquid with sufficient water to make it measure 95 cc., and filter through white paper, closely covering the funnel during filtration. Then add through the filter enough water to make the product measure 100 cc., and mix thoroughly. Keep syrup in well-stoppered bottles.

Chemical Explanation.—Lime is only sparingly soluble in water, lime water, the saturated solution, containing only 1/7 of 1 per cent of lime.

On the other hand, lime is quite soluble in water if first combined with sugar; for, in this case, a chemical combination takes place between the lime and the sugar. Such combination is called calcium saccharate, although this is scarcely correct, inasmuch as sugar contains no acid, but is an aldehyde alcohol, and the calcium compound is, therefore, similar to sodium alcoholate (see p. 659) and sodium carbolate (see p. 771).

Since the chemistry of this calcium saccharate is rather vague, no attempt will be made to work out the equation of manufacture.

Remarks on Process.—*The bright copper vessel* can be a well-scoured copper water bath. Porcelain dish not advisable, since the lime will attack the glazing.

Filter diluted liquid through white paper. The filtrate should be perfectly transparent, and must be returned through filter paper until it is clear.

In boiling the solids with water, be sure to add extra water to make up for loss of water through evaporation. If this advice is not heeded, a sticky and difficultly soluble mass results.

LINIMENTUM CALCIS—Lime Liniment

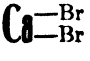
This well-known preparation *Carron oil,* has been mentioned on p. 291, while the chemistry of the preparation is referred to on p. 744. It suffices here to say that it is an emulsion of linseed oil in a lime soap, and is a valuable remedy for burns and scalds. In fact, the name Carron oil is derived from the Carron Iron Works, where it was at first largely used for burns resulting from molten metal. In case of a severe burn it is applied freely on the injured surface, and it is then covered with pads of absorbent cotton.

CALX CHLORINATA—Chlorinated Lime

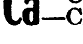
This has already been considered on p. 421, under the preparations of chlorine, where it is explained that its entire value is due to chlorine content, the lime being merely the container for the valuable gas.

It will be noticed that the preparations just discussed are considered as compounds of lime rather than as definite calcium salts, such as those we are now ready to take up.

The true salts of calcium are usually prepared by treating the carbonate with the proper acid. Thus are made calcium bromide, $CaBr_2$, and calcium chloride, $CaCl_2$, the graphic formulas of which are good demonstrations of the fact that the calcium is a dyad:



$$Ca\begin{matrix}-Br\\-Br\end{matrix}$$



$$Ca\begin{matrix}-Cl\\-Cl\end{matrix}$$

CALCII BROMIDUM—Calcium Bromide

(Calc. Bromid.)

$CaBr_2.2H_2O$. Molecular weight, 235.94

Calcium Bromide is a hydrated salt, containing not less than 84 per cent and not more than 94 per cent of $CaBr_2$.

Storage.—Preserve in air-tight containers.

Summarized Description.

White, granular, deliquescent salt; sharp, saline taste; soluble in about 0.7 part of water, and in about 1 part of alcohol. For details, see U.S.P., p. 95.

For *tests for identity,* for *impurities* (iodides, heavy metals, barium, bromate, chlorides, iron, sulfate, magnesium, alkalis) and for *assay,* see U.S.P., p. 95.

Remarks.—This compound can be made by treating calcium carbonate with hydrobromic acid by the following equation:

$$CaCO_3 + 2HBr = CaBr_2 + H_2O + CO_2,$$

or by the double decomposition of calcium hydroxide with ammonium bromide, as shown in the following equation:

$$Ca(OH)_2 + 2NH_4Br = CaBr_2 + 2NH_4OH.$$

In the former case the side-product, carbon dioxide, passes off as gas, while in the second reaction the resulting ammonium hydroxide is dissipated during the evaporation of the solution of calcium bromide.

Calcium bromide is used as a hypnotic.

Dose.—1 Gm. (15 grains).

Calcium carbonate, $CaCO_3$, is official in two forms: *prepared chalk* and *precipitated chalk.*

CRETA PRÆPARATA—Prepared Chalk

(Cret. Præp.—Drop Chalk)

Prepared Chalk is a native form of calcium carbonate freed from most of its impurities by elutriation, and containing, when dried to constant weight at 200° C., not less than 97 per cent of $CaCO_3$.

Summarized Description.

White to grayish-white fine powder, or conical drops; permanent in air; almost insoluble in water; insoluble in alcohol; soluble in some diluted acids, with effervescence and decomposition; calcines to calcium oxide. For details, see U.S.P., p. 133.

For *tests for identity*, and for *assay*, see U.S.P., p. 133.

Remarks.—This represents the native ore, which is mined in large quantities in southwest England; freed from grit by elutriation, and the resulting magma then made into the characteristic cone—prepared chalk —by the process of trochiscation (p. 138).

A characteristic quality of prepared chalk is the stickiness which it possesses, and is preferable to the precipitated chalk in diarrhea mixtures for this very reason, being more likely to adhere to the irritated mucous membrane.

Prepared chalk is a constituent of *compound chalk powder* (p. 315), and of *chalk mixture* (p. 279).

Dose.—1 Gm. (15 grains).

Whiting is an unofficial form of calcium carbonate, consisting of chalk less carefully washed than prepared chalk. School crayons formerly represented the same mineral shaped into sticks, but now most of them are made from the sulfate.

CALCII CARBONAS PRÆCIPITATUS—Precipitated Calcium Carbonate

(Calc. Carb. Præc.—Precipitated Chalk)

$CaCO_3$. Molecular weight, 100.08

Precipitated Calcium Carbonate, when dried to constant weight at 200° C., contains not less than 98 per cent of $CaCO_3$.

Summarized Description.

Fine, white, microcrystalline powder; permanent in air; almost insoluble in water; somewhat soluble in water containing ammonium salts or carbon dioxide; insoluble in alcohol; soluble in some diluted acids with effervescence and decomposition; calcined at red heat to calcium oxide. For details, see U.S.P., p. 97.

For *tests for identity*, for *impurities* (soluble impurities, heavy metals, magnesium, barium, alkalis) and for *assay*, see U.S.P., p. 97.

Remarks.—*Precipitated chalk* is made from prepared chalk by dissolving the same in hydrochloric acid, whereby calcium chloride is produced, and then precipitated by the addition of sodium carbonate to the filtered solution of calcium chloride. The process is enlarged upon below. It will be noted that the same precipitated chalk is the side product in the manufacture of the three solutions already described—solution of soda, solution of potassa, and solution of chlorinated soda. The precipitated chalk so obtained, however, is scarcely fit for use, that from the first two products being largely contaminated with alkali, while that from Labarraque's solution smells strongly of chlorine.

The chief use of precipitated chalk is as a tooth powder, and it is admirably adapted for the purpose in such preparations made by the retail pharmacist. Even better, however, is that form of calcium carbonate obtained by rubbing the soft interior of the cuttlefish bone against a sieve. As already mentioned, precipitated chalk is not as valuable as prepared chalk for diarrhea mixtures.

Dose.—1 Gm. (15 grains).

LABORATORY EXERCISE

MAKE PRECIPITATED CHALK

Marble	10 Gm.

Put in beaker and add a mixture of—

Hydrochloric acid	23 Gm.
Water	45 cc.

Watch effervescence, and when solution is complete, filter into another beaker. Then add a solution of:

Monohydrated sodium carbonate	12.4 Gm.
Water	90 cc.

Stir, let precipitate subside, then decant supernatant liquid, add more water, and finally precipitate onto a plain filter and continue washing until wash liquor no longer gives precipitate with either calcium chloride solution or silver nitrate solution. Then let precipitate dry.

Explanation.—This process is in two stages.

First, the insoluble marble (crude calcium carbonate) is dissolved in hydrochloric acid, forming soluble calcium chloride with the evolution of carbon dioxide, viz.:

Equation A:

Calcium carbonate	plus	Hydrochloric acid	give	Calcium chloride	plus	Carbon dioxide	plus	water.
$CaCO_3$	+	HCl	=		+		+	

Complete this equation.

The dissolving of marble by hydrochloric acid is for the purpose of purification, it being easier to purify substances when in solution than in solid form. The solution of calcium chloride is then treated with sodium carbonate, when calcium carbonate (precipitated chalk) separates out, while sodium chloride goes into solution.

The reaction is:

Equation B:

Calcium chloride	plus	Sodium carbonate	give	Calcium carbonate	plus	Sodium chloride.
$CaCl_2$	+	$Na_2CO_3H_2O$	=		+	

Complete this equation.

Calculations.—First, the manufacture of calcium chloride. Work out the molecular weights of calcium carbonate, hydrochloric acid, and calcium chloride, and place under equation given above. Then solve the following problems:

1. How many grams of absolute (100 per cent) hydrochloric acid needed to combine with 100 Gm. of calcium carbonate?
2. How many grams of 35 per cent hydrochloric acid needed to combine with 100 Gm. of calcium carbonate?
3. How many grams of calcium chloride will be made from 100 Gm. of calcium carbonate?

4. How many grams of 35 per cent hydrochloric acid needed to combine with 10 Gm. calcium carbonate?

Compare these figures with the recipe given above.

Now let us calculate the manufacture of calcium carbonate. Work out molecular weights of calcium chloride, calcium carbonate, and monohydrated sodium carbonate, and place these molecular weights under the equation (*B*) given above. Then solve the following problems:

1. How many grams of calcium carbonate can be made from 111 Gm. of calcium chloride?
2. How many grams of monohydrated sodium carbonate needed to combine 111 Gm. of calcium chloride?
3. How many grams of calcium carbonate can be made from 11.1 Gm. of calcium chloride?
4. How many grams of crystalline sodium carbonate needed to combine 11.1 Gm. of calcium chloride?

Compare these figures with that of the recipe given above.

Remarks on Process.—The solution of the marble and the precipitation of the chalk are described fully enough in recipe.

Decant supernatant liquid. Supernatant liquid is the clear liquid resting above precipitate. Decant it by gently tilting beaker, being careful to keep precipitate resting quietly at bottom of beaker. Use guiding rod if desired (See p. 149.)

Wash precipitate to remove all soluble salts, be they either calcium chloride or sodium carbonate. If the former is present, the silver nitrate will give a white, curdy precipitate; if sodium carbonate is there, the calcium chloride will give a white precipitate. If both are washed out and only water passes through the precipitated chalk, it will, of course, produce no precipitate with either reagent.

Dry the precipitate as you did the granulated salts (see p. 327), only, if desired, more heat can be used than with them—even the heat of a radiator or a drying oven.

CALCII CHLORIDUM—Calcium Chloride
(Calc. Chlorid.)

$CaCl_2.2H_2O$. Molecular weight, 147.03

Calcium Chloride is a hydrated salt, containing not less than 75 per cent and not more than 85 per cent of $CaCl_2$.

Storage.—Preserve in air-tight containers.

Summarized Description.

White, slightly translucent, hard fragments, or granules or sticks; sharp, saline taste; very deliquescent; soluble in about 1.2 parts of water and in about 8 parts of alcohol; fuses at red heat without decomposition. For details, see U.S.P., p. 98.

For *tests for identity*, for *impurities* (iron, aluminum, phosphates, magnesium, alkalis, heavy metals), see U.S.P., p. 98.

This substance, as already mentioned, is prepared by the treatment of calcium carbonate with hydrochloric acid, as shown in the following equation:

$$CaCO_3 + 2HCl = CaCl_2 + CO_2 + H_2O.$$

The solution is evaporated to dryness, and the product comes into the market either in the form of a white, granular powder, or in fused lumps.

Calcium chloride is of value as a desiccating agent, as an absorber of water, it being used very largely in chemical work for this purpose. Thus, in keeping the air in the case of an analytic balance free from moisture, calcium chloride is employed. It is also used as a base for freezing mixtures, for, when combined with snow, it produces the exceedingly low temperature of −48° C.

Lately it has been employed in the treatment of tuberculosis and of diseases of the respiratory tract.

Dose.—1 Gm. (15 grains).

A crystalline form of calcium chloride containing 1 molecule of the salt combined with 6 molecules of water is known and is sometimes used in medicine.

CALCII GLUCONAS—Calcium Gluconate

This new official will be discussed on p. 696.

Calcii Glycerophosphas (U.S.P. X; N.F. VI) or *Calcium Glycerophosphate* has the formula, $CaC_3H_5(OH)_2PO_4$. It is discussed at some length under Glycerophosphoric Acid (p. 680). It is the most important salt of that acid and enjoys some reputation as a nutritive tonic. *Dose.*—0.3 Gm. (5 grains).

CALCII IODOBEHENAS—Calcium Iodobehenate

This official will be discussed on p. 727.

CALCII LACTAS—Calcium Lactate

(Calc. Lact.)

$Ca(C_3H_5O_3)_2.5H_2O$. Molecular weight, 308.24

Calcium Lactate is a hydrated salt containing not less than 25 per cent and not more than 30 per cent of water. When rendered anhydrous by drying to constant weight at 120° C., it contains not less than 98 per cent of $(CH_3.CH.OH.COO)_2Ca$.

Storage.—Preserve in well-closed containers.

Summarized Description.

White, granular, efflorescent masses or powder; nearly tasteless; soluble in about 20 parts of water; almost insoluble in alcohol. For details, see U.S.P., p. 102.

For *tests for identity*, for *impurities* (heavy metals, magnesium, alkalis), and for *assay*, see U.S.P., p. 102.

Remarks.—This official is made by treating calcium carbonate with lactic acid. Like syrup of calcium lactophosphate, it is used in rachitis and in scrofulous conditions in children and for hyperacidity in adults.

Dose.—1 Gm. (15 grains).

Calcii Sulfidum Crudum (U.S.P. IX) or *Sulfurated Lime* was also called in the last Pharmacopœia, *crude calcium sulfide.* The latter name is hardly correct, as it is not pure calcium sulfide, CaS, but a mixture of this with calcium sulfate and carbon. U.S.P. VIII directed that it be prepared by heating together exsiccated calcium sulfate, sulfur, charcoal, and starch. This meant the reduction of the sulfate with the carbon of the two other ingredients, similar to the reduction process in the manufacture of sulfurous acid given on p. 456, only it is carried farther in the case of sulfurated lime, the reaction being—

$$CaSO_4 + C_2 = CaS + 2CO_2.$$

However, part of the oxygen grasped by the carbon is taken from the air. Starch was also used in the process, to furnish additional carbon as needed.

In the Pharmacopœia of 1880 the chemical was made by heating a mixture of lime and sulfur. This yielded a mixed product, for, as seen by the following reaction,

$$4CaO + S_4 = 3CaS + CaSO_4,$$

there is oxygen to be disposed of, thus giving rise to the sulfate. Sulfurated lime is a pale gray or yellowish powder, having the odor of hydrogen sulfide. It is used as an alterative in skin diseases. It is indicated in that morbid condition of the system which manifests itself in that form of eruption called boils.

Dose.—60 mg. (1 grain).

The so-called "calcium sulfide" used as a depilatory—for the removal of superfluous hair—is, in truth, calcium sulfhydrate, that is, calcium sulfide combined with an extra molecule of hydrogen sulfide. This body is made by passing hydrogen sulfide gas through a thin paste of calcium hydroxide (1 part) in water (3 parts)—this paste being commonly called *milk of lime.* The equation of reaction is

$$Ca(OH)_2 + 2H_2S = Ca(HS)_2 + 2H_2O.$$

Calcii Hypophosphis (N.F. VI) or *Calcium Hypophosphite*, $CaPH_2O_2$, is made by warming a mixture of phosphorus (finely divided, as explained on p. 139), and milk of lime at 40° C., the reaction being

$$3Ca(OH)_2 + 8P + 6H_2O = 3Ca(PH_2O_2)_2 + 2PH_3.$$

The solution of calcium hypophosphite is filtered from the excess of lime and is evaporated at low temperatures until a granular mass results.

The method of manufacture just mentioned is by no means free from danger, as mentioned when discussing the hypophosphites of potassium and sodium. Not only is the spontaneously inflammable *phosphine* (PH_3) evolved during process of manufacture, but also while granulating the salt. Hence the advice not to heat hypophosphites above 85° C. even on the water bath.

Calcium hypophosphite occurs in colorless prisms, lustrous scales or as a white crystalline powder and is soluble in 6.5 parts of water. It frequently happens that the calcium hypophosphite of commerce does not completely dissolve in the amount of water and acid directed for the manufacture of the official syrup of hypophosphites. This is due to the fact that such calcium hypophosphite is not up to the official requirements as to purity, and it is, therefore, good pharmacy always to choose a very reliable make of this salt for hypophosphite preparations. As is the case with all hypophosphites, this salt is supposed to be of value as a nutritive in phthisis. It is a constituent of *syrup of hypophosphites* and of a number of other syrups of hypophosphites of the National Formulary. (See pages 222 and 223.)

Dose.—500 mg. (8 grains).

Calcii Phosphas Precipitatus (N.F. VI) or *Precipitated Calcium Phosphate,* $Ca_3(PO_4)_2$, is obtained from bone ash, 80 to 85 per cent of which consists of this chemical.

In preparing it, bones are treated with hydrochloric acid, whereby soluble acid phosphate and calcium chloride are produced, as shown in the following equation:

$$Ca_3(PO_4)_2 + 4HCl = CaH_4(PO_4)_2 + 2CaCl_2,$$

and, on addition of ammonia water to the solution, the phosphate is again formed and precipitates out—

$$CaH_4(PO_4)_2 + 2CaCl_2 + 4NH_3 = Ca_3(PO_4)_2 + 4NH_4Cl.$$

Bone ash contains some magnesium salts, and the calcium phosphate obtained from this source is apt to contain ammonio-magnesium phosphate. For this reason much of the better grade of calcium phosphate is made by the action of sodium phosphate on calcium chloride in the presence of ammonia. If the reaction takes place in neutral solution, hydrogen calcium phosphate [$CaH_4(PO_4)_2$] is produced.

Because precipitated calcium phosphate is supposed to be practically insoluble in water, this salt was directed by the Pharmacopœia of 1890 as the diluent and divider in the making of such preparations as aromatic waters and elixirs and tincture of opium. That the salt is completely insoluble when used for this process is not so, and frequently leads to mischievous results. Waters made with the precipitated phosphate rapidly become stringy, due to microscopic plants, while the alkaloids are rendered partly insoluble, with corresponding decrease in strength of the preparation. For this reason, at the revision of 1900, purified talc was chosen for aromatic waters instead of the phosphate. The precipitated phosphate is used occasionally as a tonic in 15-grain doses.

Syrupus Calcii Lactophosphatis (N.F. VI) is discussed on p. 677, so here it suffices to say that it is made by treating calcium carbonate with lactic and phosphoric acids, along with sugar and flavor, and that it is given in 2½-drachm doses.

Calcii Sulphas Exsiccatus (U.S.P. VIII) or *Exsiccated Calcium Sulfate,* $CaSO_4$, represents the native mineral gypsum in exsiccated form, and is commercially known as *plaster of paris.* Its use in medicine and pharmacy is purely mechanical, and is due to the fact that when combined with water, it forms a paste which quickly settles to a firm mass, due to the formation of the crystalline compound, $CaSO_4.2H_2O$. This makes plaster of paris of great value in the setting of broken limbs, while its pharmaceutic use in making fast the handles of pestles has already been commented on on p. 135.

Terra alba is a white material used as a filler in cheap candy. Its use is prohibited in most pure food laws. LaWall finds that the substance used under this name is not always the same but that it is sometimes gypsum, sometimes kaolin, or even burnt alum.

STRONTIUM

Symbol, Sr. Atomic weight, approximately, 87

This element occurs in the minerals *strontianite* (strontium carbonate) and *celestite* (strontium sulfate).

The sulfate is found in considerable quantity in the group of islands in Lake Erie, especially at Put-in-Bay Island.

The carbonate was discovered near Strontian, a village of Scotland, and on being found different from barium carbonate was named by Hope, who proved it contained a new metal by preparing several salts.

The metal was first isolated in impure form by Davy in 1808 by electrolysis of the oxide; the pure metal being first obtained by Bunsen and Matthiessen in 1855. It is now made by electrolysis of the chloride.

Strontium is a brassy metal, having the specific gravity of 2.5, and comparatively stable in air. When placed in water, however, it decomposes same in a manner similar to that already explained under Potassium.

The tests for strontium and its compounds are, first, the crimson color which it transmits to a colorless flame, and, secondly, the sparingly soluble sulfate which is formed on adding a soluble alkaline sulfate to a soluble salt of strontium.

Strontium has comparatively little value in pharmacy, its chief use being in pyrotechnics. The red flame just described makes the strontium compounds valuable in this direction. Strontium is also used in the sugar industry for the regeneration of molasses.

While U.S.P. IX recognized three salts of strontium—the bromide, the iodide and the salicylate—U.S.P. XI recognizes none of these salts. The demand for the admission of strontium salts into the United States Pharmacopœia of 1890 was chiefly developed through the advertising efforts of certain firms exploiting such compounds in medicine. The unprejudiced observer finds, however, scarcely sufficient value in strontium compounds to justify official recognition.

Strontii Salicylas (U.S.P. X; N.F. VI) or *Strontium Salicylate*, $(C_6H_4.OHCOO)_2Sr.2H_2O$, is a white odorless crystalline powder made by treating strontium carbonate with salicylic acid. It is used in rheumatism.

Dose.—1 Gm. (15 grains).

Strontii Bromidum (N.F. VI) or *Strontium Bromide*, $SrBr_2$, is made by treating strontium carbonate with hydrobromic acid. It occurs in colorless, hexagonal, deliquescent crystals which are soluble in about 0.35 part of water. It is used as a hypnotic in 1 Gm. doses.

Strontii Iodidum (U.S.P. IX) or *Strontium Iodide*, SrI_2, is made by treating strontium carbonate with hydriodic acid. It occurs in hexagonal deliquescent plates or as a white granular powder and is used as an alterative in 300 mg. doses.

BARIUM

Symbol, Ba. Atomic weight, 136.4

The chief ores of this metal are *heavy spar* (barium sulfate) and *witherite* (barium carbonate). The former ore was called "barote" by Guyton de Morveau (1779), from the Greek word *baros* (heavy), and from this the name of the element was derived.

An amalgam of barium and mercury was first obtained by Berzelius and Pontin in 1808, by electrolysis, but these investigators were unable to isolate the element, this being done by Davy the same year by distilling the mercury from the amalgam.

Barium is now obtained by electrolysis of the fused chloride.

Metallic barium resembles in many ways metallic strontium. It has a specific gravity of 3.75, is a brassy metal, and, like strontium, while stable in air, reacts with water, forming hydrogen and the hydrate of the metal.

U.S.P. XI recognizes one barium compound, the sulfate.

BARII SULFAS—Barium Sulfate

$BaSO_4$. Molecular weight, 233.42

Caution.—In prescribing barium sulfate the title should always be written out in full to avoid confusion with the poisonous barium sulfide or sulfite.

Summarized Description.

White, odorless, tasteless, bulky powder; insoluble in water and organic solvents. For details, see U.S.P., p. 82.

For *tests for identity*, for *impurities* (sulfide, acid-soluble matter, soluble barium salts, phosphate, free acid or alkali, heavy metals, arsenic), see U.S.P., p. 82.

Remarks.—This official was introduced in U.S.P. X because of the demand for *barium sulfate for x-ray work*. Stomach and intestinal specialists now base their diagnosis largely upon *x*-ray photographs showing the action of a test meal as it passes through the stomach and intestines; the test meal consisting of a gruel of oatmeal or similar food stuff mixed with about 150 Gm. of pure barium sulfate.

It is obvious that for this purpose a pure salt must be employed; hence the rather severe chemical requirements set for this compound by the new Pharmacopœia. And of even greater importance is the necessity of educating both physicians and pharmacists through the Pharmacopœia of the fatal results when *barium sulfide* is dispensed instead of *barium sulfate*. A number of deaths have been reported during the past twenty years due to this blunder,.the result of carelessness of the physician in writing for "Bar. Sulf." and of the druggist dispensing, on such a prescription, the very poisonous barium sulfide. The Pharmacopœia specifically mentions that the name, *barium sulfate*, should never be abbreviated in writing a prescription and to this caution might be added another one, that the pharmacist should never dispense barium sulfide on any prescription unless he personally verifies the fact that the sulfide is desired.

The fact that while the *sulfide* is very poisonous, the sulfate is practically nontoxic seems odd at first thought. The explanation lies in the fact that barium sulfate is insoluble in the fluids of the stomach and intestines and thus the toxic action of absorbed barium compounds are avoided.

Barium Dioxide (U.S.P. 1890) is made by heating barium oxide, BaO, in a current of air. It was recognized in the former Pharmacopœia because used in making solution of hydrogen dioxide (p. 417).

RADIUM

Symbol, Ra. Atomic weight, approximately, 226

This remarkable element was isolated by Madame Curie in 1898, from *pitchblende*, a mineral found in Austria. Since then the main source of radium has passed to *carnotite*, a mineral found in Colorado and latterly to a variety of pitchblende found in the Belgian Congo, which is so much richer in radium than previously known sources that the price of the element has dropped from $120,000 a gram to $50,000 a gram. This huge cost is due to the rarity of radium in even its richest ores. Thus to obtain 1 Gm. of the element, 500 tons of carnotite has to be worked up.

In chemistry and medicine, radium is handled almost entirely in the form of its salts; the bromide being the compound found most satisfactory.

Radium and its salts have the property of emitting three types of emanations.

The *alpha particles* will penetrate slightly less than 0.1 mm. of aluminum. They are now known to be the same as helium electrons.

The *beta particles* will penetrate slightly less than 3 mm. of aluminum. They seem to be identical with negatively charged electrons.

The *gamma particles* will penetrate 20 cm. of lead. They are similar to *x*-rays.

The emission of these α, β and γ particles means the gradual disintegration of the radium atom, the ultimate residue left after disintegration being the element, lead. (See p. 406.) These remarkable properties of radium have brought about a complete revision of our ideas as to the nature of elements and of the atom. From these properties, our present ideas as to the structure of the atom (see p. 403) have been developed.

Radium has also been considered with keen interest as a possible medical agent, notably in the treatment of cancer, but up to now the results obtained have not measured up to the enthusiastic hopes of its advocates.

BIBLIOGRAPHY

Magnesium.—(History) Bunsen, A., 82, 1852, 137; Hackh, A.J.P., 90, 1918, 574; Anon., Ch. and Dr., 107, 1928, 483. (Production) Grosvenor, Jl. Ind. Eng. Ch., 8, 1916, 275; Anon., Ph. Jl., 107, 1921, 289; Harvey, Jl. Frank. Inst., 199, 1925, 725; Kiepenheuer, Jl. Soc. Ch. Ind., 45, 1926, 874B; Gann, Jl. Ind. Eng. Ch., 22, 1930, 694; Ravier, Jl. Soc. Ch. Ind., 51, 1932, 349B; De Fleury, C.A., 26, 1932, 5046. (Sources) Stone, Yearbook, A.Ph.A., 10, 1920, 342; Natarajan, Jl. Ind. Eng. Ch., News Ed., Feb., 1928, 8. (Properties) Arndt and Ploetz, C.A., 22, 1928, 2863; Eder, C.A., 25, 1931, 44. (Therapeutics) Hirschfelder and Searles, C.A., 21, 1927, 281. (Uses) Anon., Pharm. Era, 53, 1920, 368.

Flashlight.—(Composition) Ommeganck, A.Ph.A., 45, 1897, 465. (Dangers) Anon., A.J.P., 61, 1889, 640.

Magnesium Oxide.—(History) Franklin, Ph. Jl., 127, 1931, 66. (Properties) Luck, Pract. Dr., 48, Apr., 1930, 15; Deeney, A.J.P., 104, 1932, 22.

Magma of Magnesia.—(History) Lehman, Jl. A.Ph.A., 18, 1929, 261, 391 and 482. (Manufacture) Raubenheimer, A Ph.A., 55, 1907, 150; Beringer, Jl. A.Ph.A., 2, 1913, 1141; McNeary, Jl. A.Ph.A., 4, 1915, 1395; Terry and Davy, Jl. A.Ph.A., 9, 1920, 148. (Properties) Smith and Giesy, Jl. A.Ph.A., 12, 1923, 955.

Magnesium Carbonate.—(History and manufacture) Anon., Ph. Jl., 14, 1854, 221. (Composition) Engel, Comp. rend., 100, 1885, 911; Beckurts, Arch. d. Pharm., 218, 1881, 429 and 219, 1881, 13; Kolthoff, Ap. Zt., 29, 1914, 883; Nishimura, C.A., 23, 1929, 50; Menzel and co-workers, C.A., 24, 1930, 2075. (Properties) Maranne, Ph. Jl., 94, 1915, 67. (Uses) Gard and Robinson, Jl. Soc. Ch. Ind., 49, 1930, 125F.

Solution of Magnesium Citrate.—(History) Robiquet, Jl. de ph. et ch., 21, 1852, 293. (Manufacture) Snow, West. Dr., 48, Dec., 1926, 52; Stanford, Dr. Circ., 74, Feb., 1930, 46; Kleinschmidt, Pract. Dr., 49, Mch., 1931, 28. (Precipitation) Swart and Blomberg, C.A., 10, 1916, 1077; Barnby and Voight, C.A., 23, 1929, 2783; Rees, A.J.P., 102, 1930, 496. (Assay) Arny and Schaefer, Jl. A.Ph.A., 19, 1930, 941; Haussmann, A.J.P., 103, 1931, 44.

Granular Magnesium Citrate.—(Manufacture) Archibald, A.J.P., 42, 1870, 231.

Magnesium Sulfate.—(History) Kirkby, Ph. Jl., 106, 1921, 386. (Manufacture) Anon., Ph. Jl., 14, 1854, 71 and 125; Gregson, A.J.P., 18, 1847, 231; Efremov and Narkevich, C.A., 23, 1929, 2788; Dow, Jl. Ind. Eng. Ch., 22, 1930, 113; Heath, *ibid.*, 22, 1930, 437. (Palatable) Anon., Dr. Circ., 57, 1913, 520; Foran, Proc. P.P.A., 43, 1920, 151. (Confusion with zinc sulfate) Labarraque and Lecanu, A.J.P., 1, 1829, 155. (Medical uses) Cavalieri, Ph. Jl., 104, 1920, 40.

Talc.—(History) Grohmann, Ch. Zt., 43, 1919, 51. (Sources) Gunn, Merck's Rept., 19, 1910, 222; Ladoo, Dr. Circ., 64, 1920, 370 and 462. (Properties) E'we, A.J.P., 93, 1921, 316.

Calcium.—(History) Lippmann, Zt. angew. Ch., 18, 1905, 1214; Berzelius and Pontin, Gilbert's Ann., 36, 1810, 255; Davy, Gilbert's Ann., 32, 1808, 369; Hackh, 90, 1918, 573. (Isolation) Caron, A., 115, 1860, 355; Johnson, Jl. Ind. Eng. Ch., 2, 1910, 466; Anon., A.J.P., 105, 1933, 89.

Lime.—LaWall, A.Ph.A., 59, 1910, 315; Anon., Nat. Lime Assn., Brief No. 251; Woodhouse, Jl. Soc. Ch. Ind., 51, 1932, 115. (Slaking) Kosmann, Jl. Soc. Ch. Ind., 39, 1920, 446A.

Portland Cement.—Meyer, Zt. angew. Ch., 25, 1912, 711; Watson, Jl. Soc. Ch. Ind., 42, 1923, 157; Jones, C.A., 12, 1918, 2677; Leffman, Jl. Frank. Inst., 202, 1926, 253; Gessner, C.A., 23, 1929, 1237; Carter, Jl. Soc. Ch. Ind., 49, 1930, 11.

Lime Water.—(Manufacture) Cliffe, A.Ph.A., 56, 1908, 1033. (Keeping) Clark, A.Ph.A., 55, 1907, 669; Raubenheimer, A.Ph.A., 55, 1907, 179; Nitardy, A.Ph.A., 57, 1907, 85; Brown, A.Ph.A., 59, 1911, 73; Hostmann, C. U. C. P. Alumni Jl., 23, 1916, 5; Terry, C.A., 10, 1916, 91. (Therapeutics) Hommell, Pract. Dr., 46, Dec., 1928, 16.

Syrup of Lime.—(Chemistry) Lippmann, Ch. Zt., 7, 1883, 1377; Kiliani, B., 41, 1908, 2650; van Ginneken, C.A., 6, 1912, 1862; Peligot, Jl. de. ph. et ch., 19, 1851, 324; Squibb, A.J.P., 39, 1867, 335; Beral, A.J.P., 13, 1841, 74; Reinders and van Gelder, C.A., 26, 1932, 2640.

Lime Liniment.—(History) LaWall, Drug Topics, 45, July, 1929, 126. (Manufacture) Langenhan, Pract. Dr., 42, May, 1924, 25. (Therapeutics) Hommell, Pract. Dr., 47, 1929, 23.

Sulfurated Lime.—(Stability) Schmidt and Engelhardt, A.Ph.A., 58, 1910, 1005.

Prepared Chalk.—England, A.J.P., 58, 1886, 82; Nichols, A.J.P., 92, 1920, 391.

Precipitated Chalk.—Anon., A.Ph.A., 48, 1900, 710; Hill, Ph. Jl., 124, 1930, 99; 109 and 157.

Whiting.—England, A.J.P., 58, 1886, 77.

Calcium Chloride.—(Medical Uses) Denis and Minot, Dr. Circ., 64, 1920, 339; Maendl. Ph. Zt., 65, 1920, 503; Procas, Pharm. Era, 53, 1920, 241; Lake, Am. Dr., 79, May, 1929, 19; Podolsky, Pract. Dr., 49, Oct., 1931, 16. (Technical uses) Anon., *ibid.*, 53, 1920, 133.

Calcium Hypophosphite.—(History) Anon., Jl. A.M.A., 62, 1914, 1346. (Manufacture) Berlandt, Arch. d. Pharm., 171, 1865, 238. (Manufacture and properties) Janssen, Ph. Jl., [2], 3, 1862, 327. (Therapeutics) Marriott, Jl. A.M.A., 66, 1916, 486.

Calcium Phosphate.—(Structure) Gassmann, Zt. physiol. Ch., 83, 1913, 403; Klement, C.A., 24, 1930, 405. (Use as diluent) Feil, A.Ph.A., 46, 1898, 417; Arny, A.Ph.A., 46, 1898, 234.

Terra Alba.—LaWall, A.J.P., 85, 1913, 49.

Plaster of Paris.—Brittain and Elliott, Jl. Soc. Ch. Ind., 42, 1923, 154T; Haddon and Brown, Jl. Soc. Ch. Ind., 43, 1924, 11T; Budnikov and Lewin, Jl. Soc. Ch. Ind., 44, 1925, 172B; Bruère, C.A., 23, 1929, 3775; Neville, Jl. Frank. Inst., 205, 1928, 877; Emde, C.A., 23, 1929, 5211; Johnson and Gibson, C.A., 24, 1930, 1940; Casella, C.A., 24, 1930, 4356; Krauss and Jörns, C.A., 25, 1931, 1039; Gibson and Johnson, Jl. Soc. Ch. Ind., 51, 1932, 25T; Yamane, C.A., 26, 1932, 574; Haddon, Jl. Soc. Ch. Ind., 52, 1933, 24.

Strontium.—(History) Hope, Trans. Roy. Soc. Edin., 4, 1792, 3, through Gmelin-Kraut, 2^2, 1909, 125; Bunsen and Matthiessen, Jl. prakt. Ch., 107, 1869, 253. (Sources and production) Meade, Ch. News, 117, 1918, 126; Mallery, C.A., 11, 1917, 322. (Use) Brown, Handbook of Sugar Chemistry, 1913, 679; Meyer, Jl. Ind. Eng. Ch., 6, 1914, 1036. (Toxicity) Loesser and Konwiser, C.A., 24, 1930, 3831.

Strontium Nitrate.—Irvin, C.A., 11, 1917, 388; Chemnitius, C.A., 22, 1928, 3267.

Strontium Salicylate.—(Therapeutics) Blankenhorn, Jl. A.M.A., 66, 1916, 331; Hare, *ibid.*, 66, 1916, 757; Sollmann, *ibid.*, 66, 1916, 758.

Barium.—(History) Berzelius and Pontin, Gmelin-Kraut, 22, 1909, 1; Davy, Works, 1840, 112. (Source) Tranton, Jl. Soc. Ch. Ind., 51, 1932, 5.

Barium Sulfate.—(Manufacture) Lott, Jl. A.Ph.A., 17, 1928, 454. (Properties) Karaoglanow, Pharm. Weekbl., 55, 1918, 47. (Medical use) Krone, Ph. Zent., 56, 1915, 144; Bensaude and Terry, A.J.P., 90, 1918, 284. (Dangers) Anon., Ph. Jl., 102, 1919, 389; Newcomb, N.W. Dr., 28, 1920, 368; Stedem, Bull. Pharm., 34, 1920, 40.

Barium Peroxide.—Stewart and Laporte, Jl. Soc. Ch. Ind., 43, 1924, 829B; Rentschler, Jl. Ind. Eng. Ch., News Ed., Mch. 20, 1930, 16; Nogareda, C.A., 25, 1931, 2655.

Radium.—(Atomic weight) Curie, Ch. News, 96, 1907, 127. (History) Curie, Am. Chim. Phys. [7], 30, 1903, 99. (Sources) Parsons, Jl. Ind. Eng. Ch., 8, 1916, 48; Anon., Ph. Jl., 111, 1923, 324; Anon., Jl. Ind. Eng. Ch., 16, 1924, 554; Anon., Jl. Soc. Ch. Ind., 44, 1925, 175; Anon., *ibid.*, 47, 1928, 753; Cooke, *ibid.*, 48, 1929, 299; Mathy, Jl. Ind. Eng. Ch., News Ed., Oct. 20, 1929, 7; Allan, Jl. Soc. Ch. Ind., 50, 1931, 379; Anon., *ibid.*, 51, 1932, 708. (Extraction) Parsons, see above; Thews and Hemle, Jl. Ind. Eng. Ch., 15, 1923, 1159; Matignon, Jl. Frank. Inst., 200, 1925, 820; Anon., *ibid.*, 206, 1928, 110; Edit., Jl. Ind. Eng. Ch., 21, 1929, 996; Traille, Jl. Soc. Ch. Ind., 51, 1932, 1034. (Properties) Curie, Compt. rend., 127, 1898, 1215; Ch. News, 80, 1899, 269; Rutherford, Phil. Mag., [5], 47, 1899, 109; [6], 5, 1903, 445 and 576; [6], 7, 1904, 202; Kelvin, *ibid.*, [6], 7, 1904, 220; Darwin, Radium, 16, 1921, 53; Millikan, Science, 54, 1921, 1; Pope, Jl. Soc. Ch. Ind., 42, 1923, 53 and 73; Hindes, Ph. Jl., 123, 1929, 233; Curie, Jl. Frank. Inst., 209, 1930, 484.

CHAPTER XXIX

ZINC, MANGANESE, COBALT, AND NICKEL

REFERRING to the chapter on Analytic Chemistry (p. 1002), it will be seen that the alkaline metals, lithium, potassium, sodium, and the radical ammonium, form the first of the seven groups into which metals are divided in analysis. The alkaline earth metals, magnesium, calcium, strontium, and barium, form the second analytic group—those precipitated from solution by ammonium carbonate and ammonium phosphate.

The third analytic group includes the metals zinc, manganese, cobalt, and nickel; these four elements, along with aluminum, iron, and chromium, being precipitated from alkaline solution by the ammonium sulfide test solution.

The last three metals form the fourth analytic group, the third and fourth groups being differentiated by the fact that the fourth group can be precipitated from acid solution by the addition of ammonia water, while the third group is not precipitated by that reagent.

With the metals considered in this chapter we reach what might be called the commercial metals—that is, those which, by reason of stability, abundance, and general utility, are used largely in the arts as metals. The isolation of these metals from their ores has been practiced for many centuries, and the process of extraction now in vogue is largely a modification of ancient methods. The study of the various methods of isolation forms the art called *metallurgy.*

ZINC

Symbol, Zn. Atomic weight, approximately 65

Zinc occurs as *calamine* (zinc carbonate) and *zinc blende* (zinc sulfide). Calamine is largely mined in the neighborhood of Aix-la-Chapelle, Germany, and it is interesting that in that neighborhood there grows a wild violet which is characterized by the large amount of zinc in its ash, and it is, therefore, given the botanic name of *Viola calaminaris.* In this country zinc is mined at Joplin, Mo., at Franklin, N. J., and at Palmerton, Pa.

Zinc was early used as a constituent of brassy alloys, the coins of the Roman emperors, Nero and Hadrian, containing it.

For this purpose an ore of zinc was evidently used, Dioscorides and Pliny calling an ore that would turn copper yellow *cadmia.* Ore for similar purposes is called by Arabian writers *climia,* and from this word come such modifications as *calimia* and *lapis calaminaris.* The word zinc is first found in the writings of Basil Valentine and of Paracelsus, but the metal does not seem to have been isolated in Europe until Henkel produced it by a secret process, although Labavius (1597) describes the metal as a peculiar tin from East Indies.

Zinc is made by roasting calamine with charcoal and distilling the resulting zinc. Since calamine is a carbonate, extreme heat will calcine it, with the formation of zinc oxide. If charcoal be present during the calcination, it will act as a reducing agent, removing the oxygen in the form of carbon monoxide and carbon dioxide, by the following reaction:

$$ZnCO_3 + C = Zn + CO + CO_2.$$

This leaves metallic zinc in a more or less impure form, and the metal is, therefore, purified by continuing the heat until the zinc distils over.

If zinc sulfide is the ore employed, it is first roasted in air, when it decomposes into zinc oxide and sulfur dioxide, the latter passing off into the air or being collected in a Gay Lussac tower. The remaining zinc oxide is treated with charcoal, as in the case of calamine.

In technic there are several processes—English, Belgian, and Silesian—these differing only in the apparatus wherein occurs the reduction of the oxide with charcoal.

Zinc occurs in several forms, such as sticks, mossy zinc, and sheet zinc, or in the form of a very fine powder. All these forms are used either for the manufacture of the official zinc salts or for the production of hydrogen.

In the latter case zinc is largely used for the purpose of making arsenic tests, and it is essential that the metal so used should be free from arsenic and other impurities found largely in the ordinary commercial zinc.

Hydrogen can be produced from zinc in two ways:

Treatment of zinc with a diluted acid:

$$Zn + H_2SO_4 = H_2 + ZnSO_4.$$

Treatment of zinc with a strong alkali:

$$Zn + 2NaOH = H_2 + Na_2ZnO_2.$$

These two reactions will be again mentioned in the chapter on Arsenic (p. 579), so here we need only touch upon that interesting compound, sodium zincate, Na_2ZnO_2. Reference to the tests for zinc salts shows the fact that any soluble zinc salt—say, zinc sulfate—when treated with a solution of an alkali—say, sodium hydroxide—yields a white precipitate which will dissolve on addition of an excess of alkali.

The first stage of this reaction is as follows:

$$ZnSO_4 + 2NaOH = Na_2SO_4 + Zn(OH)_2,$$

the white precipitate being zinc hydroxide.

When more sodium hydroxide is added to this, the precipitate is dissolved by reason of the formation of soluble sodium zincate by the following reaction:

$$Zn(OH)_2 + 2NaOH = Na_2ZnO_2 + 2H_2O.$$

Zincate of sodium, when largely diluted with water, decomposes, sodium hydroxide being produced, and zinc hydroxide being precipitated by the following equation:

$$Na_2ZnO_2 + H_2O = Zn(OH)_2 + 2NaOH.$$

Stress is here laid upon these combinations of zinc salts with alkalis because similar combinations occur when aluminum, manganese, chromium, and, to a lesser extent, iron, are treated with alkalis, this showing that such metals as zinc, aluminum, manganese, chromium, and even iron can act either as positive or negative elements, according as they are associated with elements more positive or negative than themselves.

Zinc is a valuable metal for use in the arts by reason of its power of resistance against the atmospheric change. It is true that when a fresh layer of zinc is exposed to the air, it loses its luster and becomes covered with a white layer. This layer consists of a mixture of zinc oxide and zinc carbonate, which acts as an admirable protective for the metal underneath, in a way similar to that already explained concerning the protective power of lead sulfate in the lead-chamber process. By reason of the superior stability of zinc, as compared with iron, it is quite largely used for the plating of iron utensils, such zinc-coated iron being called *galvanized iron.*

The tests for zinc and its compounds are: ammonium sulfide produces a white precipitate of zinc sulfide when brought in contact with a solution of zinc salt. This explains the value of zinc oxide paint. The other chemical largely used as a white pigment is lead carbonate, and this so-called "lead paint" possesses the objection of blackening when coming in contact with hydrogen sulfide, that reagent thereby producing the black lead sulfide. Therefore, in places where hydrogen sulfide abounds, such as chemical laboratories or lavatories, the zinc paints are preferable.

Any alkaline hydroxide produces a flocculent precipitate of zinc hydroxide with any soluble zinc salt, this precipitate redissolving in excess of alkali. Any soluble carbonate precipitates any zinc salt as a dense white zinc carbonate.

Zincum (U.S.P. IX) is the pure metal in any of the several forms mentioned above.

The following salts of zinc and their preparations are official:

Zinc acetate. At least 99.5 per cent absolute $Zn(C_2H_3O_2)_2.2H_2O$.
Zinc chloride. At least 95 per cent absolute $ZnCl_2$.
Zinc oxide. At least 99 per cent absolute ZnO.
Ointment of zinc oxide containing 20 per cent zinc oxide.
Zinc stearate. $Zn(C_{18}H_{35}O_2)_2$ admixed with traces of zinc palmitate.
Zinc sulfate. At least 99.5 per cent absolute $ZnSO_4.7H_2O$.

Salts of zinc are usually made from the metal or from the oxide, by treatment with the proper acid. Zinc is a bivalent, even as are alkaline earths (p. 513).

ZINCI ACETAS—Zinc Acetate

(Zinc. Acet.)

$Zn(C_2H_3O_2)_2 2H_2O$. Molecular weight, 219.46

Zinc Acetate contains not less than 83.16 per cent and not more than 87.32 per cent of $(CH_3.COO)_2Zn$, corresponding to not less than 99.5 per cent of the hydrated salt $[(CH_3.COO)_2Zn.2H_2O]$.

Storage.—Preserve in air-tight containers.

Summarized Description.

Soft, white, lustrous six-sided monoclinic plates; faint acetous odor; astringent, metallic taste; efflorescent and partly decomposed when exposed to air; soluble in about 2.3 parts of water and in about 24 parts of alcohol; dissociates on high heat, leaving zinc oxide. For details, see U.S.P., p. 430.

For *tests for identity* and for *impurities* (arsenic, heavy metals, alkalis, and alkaline earths), see U.S.P., p. 430.

Remarks.—This salt is made by dissolving zinc oxide in acetic acid, as shown in the following equation:

$$ZnO + 2HC_2H_3O_2 = Zn(C_2H_3O_2)_2 + H_2O.$$

Zinc acetate is a mild astringent, of considerable value in the manufacture of eye washes and gonorrheal injections. For the latter purpose a favorite prescription is one combining lead acetate and zinc sulfate. When the solutions of these two salts are mixed, a double decomposition occurs in the formation of zinc acetate, which remains in solution, and lead sulfate, which precipitates out (p. 1062).

Zinc acetate is rarely given internally.

ZINCI CHLORIDUM—Zinc Chloride

(Zinc. Chlorid.)

$ZnCl_2$. Molecular weight, 136.29

Zinc Chloride contains not less than 95 per cent of $ZnCl_2$.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

White, or nearly white granular powder, or porcelain-like masses or pencils; intensely caustic; very deliquescent; soluble in about 0.25 part of water and in about 1 part of alcohol; soluble in glycerin; at high heat is partly volatilized and partly decomposed. For details, see U.S.P., p. 431.

For *tests for identity,* for *impurities* (excess of oxychloride, heavy metals, ammonium salts, sulfate) and for *assay,* see U.S.P., p. 431.

Remarks.—This salt is made by treating metallic zinc with hydrochloric acid, as shown in the following equation:

$$Zn + 2HCl = ZnCl_2 + H_2.$$

The solution of chloride thus produced is evaporated to dryness and placed in warm dry bottles.

Zinc chloride is used chiefly externally as an antiseptic, disinfectant, and caustic. For the latter purpose it enjoyed considerable repute in cases of cancer, a preparation largely used in France—*paté de Canquoin*—being a pasty mass of flour with which is incorporated zinc chloride.

Liquor Zinci Chloridi (U.S.P. X) or *Solution of Zinc Chloride* is an aqueous solution containing not less than 48.5 per cent and not more than 52 per cent of $ZnCl_2$. Complete details of the manufacture of this solution, called *Burnett's disinfecting fluid*, including the recipe of U.S.P. X are given below. It is made by treating zinc with hydrochloric acid, evaporating the solution to dryness, adding before evaporation a small quantity of nitric acid, fusing the mass, and then redissolving it in sufficient cold water to make the official liquid contain about 50 per cent of zinc chloride. The addition of nitric acid prior to fusing is to insure the removal of traces of iron which usually contaminate the commercial metallic zinc, and in this preparation the latter is frequently employed, instead of the official chemically pure metal. Under the treatment just given the zinc chloride undergoes no change, but the iron chloride will be converted into Fe_2O_3, which is insoluble in water.

LABORATORY EXERCISE

MAKE SOLUTION OF ZINC CHLORIDE

Recipe.—

Zinc (granulated)	12.0 Gm.
Hydrochloric acid	42.0 Gm.
Nitric acid	0.6 Gm.
Precipitated zinc carbonate	0.6 Gm.
Distilled water, a sufficient quantity,	
To make about	50.0 Gm.

To the zinc, contained in a glass or porcelain vessel, add 8 cc. of distilled water; then gradually add the hydrochloric acid, and digest until reaction ceases and the acid is saturated. Pour off the solution, add the nitric acid, and heat the solution at a temperature not exceeding 115° C., until a portion, if removed and cooled, solidifies. Allow it to cool, and dissolve the solidified mass in a sufficient quantity of distilled water to make the product weigh 50 Gm. Then add the precipitated zinc carbonate, agitate the mixture occasionally during twenty-four hours, and set it aside until it has become clear by subsidence. Finally, separate the clear solution by decantation or by means of a syphon.

Chemical Explanation.—Zinc chloride is made by treating zinc with hydrochloric acid, the reaction being as follows:

Zinc plus Hydrochloric acid give Hydrogen plus Zinc chloride.
Zn + HCl = +

Complete this equation.

As this solution is supposed to be made from commercial zinc, and as this *usually* contains iron, the iron chloride produced when such metal is dissolved in hydrochloric acid must be removed from the solution. This is accomplished by adding nitric acid, evaporating the solution, and finally fusing the dry mass. Neither nitric acid nor fusion affects the zinc chloride, while nitric acid and fusion convert the ferric chloride into insoluble ferric oxide, and when the fused mass is treated with water, the zinc chloride dissolves, leaving the ferric oxide as an insoluble residue.

The solution is too caustic to be filtered through paper, so the ferric oxide is removed by sedimentation, precipitated zinc carbonate being added to aid in the clarification.

Calculations.—Figure out the molecular weights of hydrochloric acid and of zinc chloride, and give the atomic weight of zinc, and with these figures work out the following examples:

1. How many grams of zinc and absolute (100 per cent) hydrochloric acid needed to make 136 Gm. zinc chloride?
2. How many grams of 35 per cent hydrochloric acid needed to make 136 Gm. zinc chloride?

3. How much zinc chloride in 50 Gm. solution of zinc chloride, U.S.P., if this solution contains 50 per cent of the salt?

4. How much zinc and 35 per cent hydrochloric acid needed to make 25 Gm. of zinc chloride?

5. Then how much zinc and 35 per cent hydrochloric acid needed to make 50 Gm. solution of zinc chloride, U.S.P.?

Compare with quantities given in above recipe.

Remarks on Process.—The recipe just given is substantially the one given in U.S.P. IX.

Place zinc in Erlenmeyer flask, and add thereto the water and the acid.

Digest mixture by letting stand several hours in a warm place—say, on a radiator or at back of stove. Note evolution of hydrogen gas as the zinc dissolves in the hydrochloric acid.

Pour off solution (instead of filtering) into a beaker or 8-ounce wide-mouthed bottle, and evaporate to dryness in small evaporating dish on sand bath. If the dish is not large enough to hold all the solution at one time, add part at first, and when this has evaporated, add the rest. When mass is dry,

Fuse cautiously, so as to not exceed the pharmacopœial temperature, else the zinc chloride loses chlorine and decomposes. A thermometer is not necessary, however, if the mass is cautiously fused over a Bunsen burner.

Dissolve fused mass in about 25 cc. distilled water, and transfer to tared Erlenmeyer flask. Wash out dish with 5 to 10 cc. water, and use this water for bringing the weight of the solution in Erlenmeyer up to 50 Gm.

Separate clear solution by decantation. A syphon is suitable only when a large quantity is made.

ZINCI OXIDUM—Zinc Oxide

(Zinc. Oxid.)

ZnO. Molecular weight, 81.38

Zinc Oxide, when freshly ignited, contains not less than 99 per cent of ZnO.

Summarized Description.

Fine, amorphous, white, or yellowish-white powder, free from grit; absorbs carbon dioxide from the air; insoluble in water or in alcohol; soluble in diluted acids without effervescence; soluble in ammonia water and in ammonium carbonate solution; turns yellow on heating. For details, see U.S P., p. 432.

For *tests for identity*, for *impurities* (iron and other metals, excess of alkali, lead, carbonate, arsenic) and for *assay*, see U.S.P., p. 432.

Remarks.—This is prepared by the calcination of pure zinc carbonate. It is important for the pharmacist to understand the distinction between the commercial zinc oxide, which is so largely used, and the form recognized by the Pharmacopœia. The commercial form is not made by the calcination of zinc carbonate, but by the roasting of crude metallic zinc in a current of air, whereby the resulting zinc oxide sublimes. This form of zinc oxide is used very largely as a paint, and should never be used by the careful pharmacist in making the official zinc salve.

Commercial zinc oxide is of dead white tint, and is more or less gritty, while the official compound has a slightly cream tint. Were it universally employed by the pharmacist for making the official zinc ointment, there would be less complaint about the grittiness of that preparation.

Two synonyms of zinc oxide are worthy of passing notice as relics of the days of alchemy. The chemical is sometimes called *lana philosophica* (philosopher's wool), because the sublimed zinc oxide collects on the condenser in woolly tufts. The other synonym, *nihilum album*, is an interesting illustration of corruption in words in the course of time. The Latin words nix album (white snow) were coined by some poetic alchemist because of the similarity of sublimed zinc oxide to snowflakes. The term, in being used by another author, was misunderstood and written as "nichts album" (white nothing), which term was found in several books of the seventeenth century. Later some careful student decided the term "nichts album," combining as it did German and Latin, should be placed in correct Latin, and thus the form "nihilum album" (white nothing) originated. It is also called *flores zinci*.

Zinc oxide is used almost entirely externally, and so used it is a mild, healing astringent. It is chiefly applied in the form of the official *ointment.* (See p. 369.)

ZINCI STEARAS—Zinc Stearate

(Zinc. Stear.)

Zinc Stearate is a compound of zinc with variable proportions of stearic acid and palmitic acid, corresponding to not less than 13 per cent and not more than 15.5 per cent of ZnO.

Summarized Description.

Fine, white, bulky powder; faint characteristic odor; insoluble in water, alcohol or ether; fuses on heating, then burns, leaving residue of zinc oxide. For details, see U.S.P., p. 432.

For *tests for identity,* for *impurities* (alkalis, alkaline earths) and for *assay,* see U.S.P., p. 432.

Remarks.—This official is a zinc stearate containing traces of zinc palmitate. It is made by treating a solution of sodium or ammonium stearate with a solution of zinc acetate or sulfate, collecting the precipitate, and washing carefully. The sodium stearate is made by treating stearic acid with a hot solution of sodium carbonate.

The resulting white powder is used for skin troubles in the form of an ointment. It is also used as a dusting powder. Its indiscriminate use as a baby powder is dangerous, fatal results having been reported.

ZINCI SULFAS—Zinc Sulfate

(Zinc. Sulf.)

$ZnSO_4.7H_2O$. Molecular weight, 287.55

Zinc Sulfate contains not less than 55.86 per cent and not more than 58.63 per cent of $ZnSO_4$, corresponding to not less than 99.5 per cent of the hydrated salt ($ZnSO_4.7H_2O$).

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless, efflorescent, rhombic crystals or granular powder; astringent metallic taste; soluble in about 0.6 part of water and about 3 parts of glycerin; insoluble in alcohol; partly dissociated by strong heat. For details, see U.S.P., p. 433.

For *tests for identity,* for *impurities* (heavy metals, arsenic, free acid, alkalis and alkaline earths) and for *assay,* see U.S.P., p. 433.

Remarks.—Zinc sulfate (or *white vitriol*) is made on a large scale by roasting the ore, zinc blende (zinc sulfide). The oxygen of the air combines with the heated zinc sulfide, forming zinc sulfate, as shown in the following equation:

$$ZnS + O_4 = ZnSO_4.$$

The sulfate is separated from the extraneous mass of silica and other metals by lixiviation and is then crystallized.

It is also made by treating zinc oxide or metallic zinc with sulfuric acid. Commercial zinc contains iron and other metals, and these are removed from the acid solution by digesting with an excess of zinc, saturating the solution with chlorine gas, and then adding precipitated zinc carbonate. The filtered solution is then evaporated to drive off chlorine and to concentrate to the point at which the sulfate will begin to crystallize.

Zinc sulfate is a very valuable astringent, for which purpose it is given internally in doses of from 1 to 2 grains. In doses five times as great it is an emetic, and is used considerably in evacuating the stomach in cases of poisoning. For ordinary purposes of emesis it is too irritating, and ipecac is preferable. Externally, zinc sulfate solution is used as an astringent wash, particularly in cases of gonorrhea.

Dose.—As emetic, 1 Gm. (15 grains).

When solutions of zinc sulfate and barium sulfide are mixed together in molecular proportions a heavy white precipitate is formed. This upon drying yields the pigment *lithopone* which contains approximately 30 per cent of zinc sulfide and 70 per cent of barium sulfate.

Zinci Bromidi (U.S.P. VIII) or *Zinc Bromide*, $ZnBr_2$, is made by either one of two ways: a solution of zinc sulfate is treated with a solution of potassium bromide, the potassium sulfate separated from the solution of zinc bromide by the addition of alcohol (see Ammonium Iodide, p. 508). A better method, however, is by treating bromine placed under a considerable layer of water with granulated zinc, the reaction being as follows:

$$Zn + Br_2 = ZnBr_2.$$

In both cases the salt is obtained from the solution by granulation.

Medical Properties.—Zinc bromide is used as a hypnotic in epilepsy in 2-grain doses.

Zinci Carbonas Præcipitatus (U.S.P. IX) or *Precipitated Zinc Carbonate* is a compound of variable composition.

It, like the official magnesium carbonate and lead carbonate, is a mixture of the true carbonate with the hydroxide. Like magnesium carbonate, the proportion of the carbonate to the hydroxide depends on conditions of precipitation—on concentration of solutions, temperature, and proportion of the two chemicals used in manufacture.

The official carbonate is made by mixing hot solutions of zinc sulfate with sodium carbonate. If cold diluted solutions of the two salts are mixed, the normal carbonate is produced, but during the reaction considerable carbonic acid is evolved, and the carbonate thus produced dissolves in this carbonated water. Hence the process is wasteful, and in factories recourse is always had to the process of hot precipitation. The normal carbonate, moreover, is unstable, producing, on drying, the official carbonate.

It is an impalpable, tasteless, white powder, that is insoluble in water, but soluble in acids with effervescence. It is used chiefly externally as a dusting powder, being mildly astringent.

Zinci Iodidum (N.F. VI) or *Zinc Iodide*, ZnI_2, is made by combining metallic zinc with iodine, as shown in the following equation:

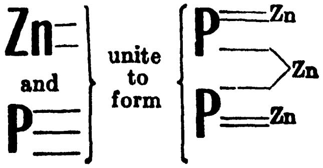
$$Zn + I_2 = ZnI_2.$$

This can be done by combining the two elements dry and subliming the resulting zinc iodide, or the elements can be digested under water and zinc iodide obtained in crystals by evaporation of the solutions.

This salt is used as an alterative. *Dose.*—65 mg. (1 grain).

Oleatum Zinci (U.S.P. 1890) or *Oleate of Zinc* is made by sifting zinc through a fine sieve into oleic acid contained in an evaporating dish, and warming until the oxide is dissolved. As already explained under the head of Oleates, this chemical can be considered as a pharmaceutical—as a solution of zinc oleate in a large excess of oleic acid. It is referred to here in order to emphasize the distinction between it and the true *zinc oleate*. While the pharmaceutical oleate of zinc is in the form of a thin, greasy liquid, the definite chemical, zinc oleate, is a smooth white powder, and is made by mixing solutions of Castile soap and zinc sulfate. It is used in a manner similar to zinc oxide, but by some specialists is preferred to the latter for dusting purposes.

Zinci Phosphidum (U.S.P. 1890) or *Zinc Phosphide* is made by passing the vapor of phosphorus over powdered zinc in an atmosphere of hydrogen. The performance of this operation, it is needless to say, required the utmost caution. The zinc is placed in a tube of Pyrex glass, the air having been carefully excluded by passing hydrogen through the tube. The phosphorus is then distilled from the retort, from which the air has also been removed by means of hydrogen, and under such circumstances the two elements combine without danger. Zinc phosphide affords an interesting problem of linking by valence:



or Zn_3P_2

It is nearly five times heavier than water.

Zinc phosphide is a nervous stimulant and aphrodisiac, and is administered in doses of from 3 to 8 mg.

Zinci Phenolsulfonas (N.F. VI) or *Zinc Sulfocarbolate,* $(C_6H_5OSO_3)_2Zn$, is made by treating barium sulfocarbolate with zinc sulfate, when barium sulfate precipitates, leaving zinc sulfocarbolate in solution. By evaporation of this solution the salt is obtained in crystals, The manufacture of barium sulfocarbolate has already been described on p. 495. The salt can also be made by preparing phenolsulfonic acid (p. 775) and then adding the molecular quantity of zinc sulfate thereto, the zinc phenolsulfonate crystallizing from the mixture.

Zinc phenolsulfonate occurs in colorless rhombic prisms, tabular crystals or granular powder, that turn pink on exposure to air. It is soluble in about 1.6 parts of water and in about 1.5 parts of alcohol. It is a useful astringent antiseptic and is employed in 125 mg. doses.

Zinci Valeras (U.S.P. IX) or *Zinc Valerate,* $Zn(C_5H_9O_2)_2$, is made by double decomposition between sodium valerate and zinc sulfate. It occurs in pearly scales or white powder having the odor of valerian and is a useful nervine and antispasmodic. *Dose.*—125 mg. (2 grains).

MANGANESE

Symbol, Mn. Atomic weight, approximately 55

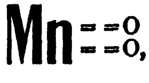
The chief ores of manganese are *pyrolusite* (MnO_2), *braunite* (Mn_2O_3), *hausmannite* (Mn_3O_4), and *manganese spar* ($MnCO_3$).

While manganese affords only one pharmacopœial salt, *potassium permanganate,* three salts of this metal are recognized in N.F. VI. A word as to the origin of its name which is similar to another element, magnesium, and to the term "magnet." In the days of Pliny, at the beginning of the Christian era, three products bearing the name magnesia were known, all coming either from the province of Magnesia, on the borders of Macedonia, or from the country around the city of Magnesia in Asia Minor. Pliny describes all three. One was white (our present magnesium carbonate), one was black and attracted iron (magnetic iron ore), while a third was brown and was used in glass making (manganese dioxide). That form attracting iron was rechristened magnet before the days of Avicenna (A. D. 980–1037), for in his medical writings we find a chapter on magnets, entitled "de Magnete." The distinction in the name manganese and magnesium was not made until the beginning of last century, after both elements had been isolated.

Manganese is obtained by the reduction of the oxide with charcoal at red heat.

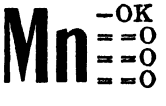
It is a gray white, hard metal, having the specific gravity of 7.2. It is, like zinc, comparatively stable in air, although it does oxidize in moist air, and more quickly when immersed in water. Manganese bronze (p. 594) is a very durable alloy.

Manganese is an element whose valence shows interesting variation. In manganese sulfate, $MnSO_4$, its valence seems to be II; in manganese dioxide, MnO_2, the valence of the metal is IV—



$$\mathrm{Mn}\begin{array}{l}=\!=\mathrm{O}\\=\!=\mathrm{O},\end{array}$$

while in potassium permanganate, $KMnO_4$, manganese shows the valence VII; the graphic formula of the compound being—



$$\mathrm{Mn}\begin{array}{l}-\mathrm{OK}\\=\!=\mathrm{O}\\=\!=\mathrm{O}\\=\!=\mathrm{O}\end{array}$$

Manganese, like zinc, seems to occupy a position between the nonmetallic and the metallic elements. It has been shown that when zinc is combined with strong alkalis, zincates are formed, the zinc hydroxide in that case acting as an acid. Still more striking is the case with manganese oxides, particularly those showing the valence VI and VII, permanganic acid, $HMnO_4$, being as distinctly acid as is perchloric acid ($HClO_4$). Yet the manganese with lower valence has basic properties, and when the metal is treated with acid, it yields a manganese salt in which the element shows the valence II.

Tests.—Manganese is interesting to the chemist as affording a large variety of very beautiful tests. When a soluble salt of manganese is treated with ammonium sulfide solution, a flesh-colored precipitate of manganese sulfide is produced. This precipitate is notable as the only flesh-colored sulfide. If a trace of manganese salt is added to a borax bead (see p. 997), a beautiful amethyst color is transmitted to the same. If any manganese salt is fused with a mixture of potassium nitrate and sodium carbonate on a piece of platinum foil, green sodium or potassium manganate is formed, as shown in the following equation:

$$MnO_2 + Na_2CO_3 + KNO_3 = KNO_2 + CO_2 + Na_2MnO_4.$$

If this green manganate be boiled with water, a pink solution of the permanganate is formed by the following reaction:

$$3Na_2MnO_4 + 2H_2O = 2NaMnO_4 + MnO_2 + 4NaOH.$$

Crum's test also exhibits the same purple color, due to permanganic acid. It is as follows: if a manganese salt is treated with plumbic oxide and nitric acid, permanganic acid is formed, as shown in the following equation:

$$2MnSO_4 + 5PbO_2 + 6HNO_3 = 2HMnO_4 + 2PbSO_4 + 3Pb(NO_3)_2 + 2H_2O.$$

The same reaction occurs if red lead or if litharge is used instead of plumbic oxide.

The only manganese compound that is official in the present pharmacopœia is potassium permanganate.

Mangani Dioxidum Præcipitatum (U.S.P. IX) or *Precipitated Manganese Dioxide*, MnO_2, was formerly recognized as a substitute for the crude ground ore, pyrolusite, the form of manganese dioxide that was formerly official. The synthetic form is made by precipitating manganous sulfate with ammonia water in the presence of hydrogen dioxide solution. Were manganous sulfate precipitated with ammonia water alone, manganous oxide (MnO) would result; hence the use of the oxidizing agent, hydrogen dioxide.

Precipitated manganese dioxide occurs in the form of a heavy very fine black powder, that is insoluble in water. It is used for anemia, particularly that type which arises from female complaints. It is administered preferably by filling capsules with the prescribed amount of the binoxide in fine powder. *Dose.*—250 mg. (4 grains).

Mangani Glycerophosphas (N.F. VI) or *Manganese Glycerophosphate*, $MnC_3H_5(OH)_2PO_4$, is made by treating manganese carbonate with glycerophosphoric acid (p. 681). It is frequently made more soluble by the addition of a small amount of citric acid. It is one of the ingredients of *compound elixir of glycerophosphates*, N.F. (p. 229). *Dose.*—0.2 Gm. (3 grains).

Mangani Citras Solubilis (N.F. VI) or *Soluble Manganese Citrate*, $[C_3H_4OH(COO)_3]_2Mn_3$, is manganese citrate rendered soluble by the presence of sodium citrate. It contains from 48 to 52 per cent of the anhydrous manganese salt. It is one of the ingredients of solution of peptonized iron and manganese, N.F. (pages 213 and 950). *Dose.*—3 grains.

Mangani Hypophosphis (N.F. VI) or *Manganese Hypophosphite* $Mn(PH_2O_2)_2 + H_2O$, is made by mixing a solution of manganese oxalate with a solution of calcium hypophosphite and evaporating the filtrate on a water bath to a granular powder.

It is a constituent of *compound syrup of hypophosphites*, N.F., and is used as a tonic, in 3-grain doses.

Mangani Sulfas (U.S.P. VIII; N.F. IV) or *Manganese Sulfate*, $MnSO_4 + 4H_2O$, is made by treating binoxide of manganese with carbon at red heat, whereby it is reduced to manganous oxide, MnO, as shown in the following equation:

$$2MnO_2 + C = CO_2 + 2MnO.$$

The manganous oxide is made into paste with sulfuric acid and heated to redness, when manganese sulfate is formed, as shown in the following equation:

$$MnO + H_2SO_4 = H_2O + MnSO_4,$$

and goes into solution and is purified by crystallization.

Manganese sulfate is used as a tonic, similar to the iron preparation, and is also used for gout. Its dose is 3 grains.

POTASSII PERMANGANAS—Potassium Permanganate

This salt has been considered under the potassium compounds (see p. 472), so here we need only again call attention to the synonym, *mineral chameleon*, it being so called because of the changes in tint which the permanganate exhibits under treatment with various reagents.

COBALT AND NICKEL

As neither of these metals, nor any of their compounds, is recognized by the Pharmacopœia, they can be briefly considered together.

Cobalt, called from the German *Kobold*, because the miners working in cobalt ores found the same difficult to extract, and attributed this difficulty to the influence of the kobolds, mischievous imps supposed to inhabit mines. It occurs in the form of a silvery metal that is now being used in making rustless alloys. One of these, *stellite*, an alloy of cobalt or nickel with chromium and tungsten, resembles platinum in appearance and is used in making crucibles, evaporating dishes and spatula blades.

Of its compounds, the silicate is of a striking blue color, and is used in painting and decorating under the name of *smalt;* the chloride, $CoCl_2$, occurs in the form of pink crystals, which comparatively easily effloresce and in so doing will change to a blue tint. For this reason the solution of cobalt chloride has been suggested for *invisible ink* or *sympathetic ink*, the writing appearing practically colorless until heated, when the effloresced salt develops itself in blue tracery. It is also used in the manufacture of cheap paper barometers, consisting of bibulous paper dipped into a solution of cobalt chloride and dried. In moist weather this paper appears to be pink, whereas on drying it becomes blue through the efflorescence of the salt.

Metallic nickel is very largely used. It is of value for cooking utensils, although for this purpose it is somewhat costly, while the use of nickel coins is so extensive as to require no additional comment. The coating of utensils with the metal by electric deposition (*nickel plating*) is also well known, nickel being used in such cases because it does not easily tarnish.

A valuable alloy of nickel is *German silver*. This consists of 50 per cent of copper and 25 per cent each of zinc and of nickel. This alloy possesses a silvery tint, and was formerly largely used as the metallic trimming of glass show-cases. *Monel metal* is a valuable alloy consisting of approximately two thirds nickel and one third copper while *ni-chrome* is an alloy of nickel and chromium. It is a rustless metal used in making wire gauze (see p. 88) and in numerous other ways.

By an *alloy* we mean a solution of several metals with each other while in a fused state. Such alloys frequently possess valuable properties not shown by their constituents, and many alloys of great value will be discussed on later pages.

BIBLIOGRAPHY

Zinc.—(History) Hommel, Ch. Zt., 36, 1912, 905 and 918; Lippmann, Zt. angew. Ch., 18, 1905, 1212; Hackh, A.J.P., 90, 1918, 478; Djang, C.A., 20, 1926, 1342; Anon., Jl. Soc. Ch. Ind., 49, 1930, 1074; Dyson, Ph. Jl., 128, 1932, 163. (Sources) U. S. Geological Survey Rep., 22, Pt. II, 1900; Bentell and Matzke, C.A., 9, 1915, 2495. Palache, C.A., 23, 1929, 1082. (Smelting) Dyson, see above; Seiffert and co-workers, C.A., 25, 1931, 5121.

Zinc Bromide.—(Manufacture) Anon., A.Ph.A., 28, 1880, 222. (Uses) Joynes, A.J.P., 45, 1873, 366.

Zinc Carbonate.—(Composition) Redwood, Ph. Jl., 2, 1843, 506; Davs, C.A., 23, 1929, 50.

Zinc Chloride.—Efremov and Yakimetz, C.A., 22, 1928, 3962; Chemnitius, C.A., 24, 1930, 1707.

Solution of Zinc Chloride.—Krantz, Proc. Md. Ph. Assn., 41, 1923, 59.

Zinc Oxide.—(Manufacture) Anon., A.Ph.A., 26, 1878, 400; Adadurov, C.A., 22, 1928, 3306; Daniels, C.A., 23, 1929, 242. (Synonyms) Arny, Am. Dr., 34, 1901, 3; Würth, Ch. Zt., 54, 1930, 201.

Zinc Phosfide.—(Manufacture) Jolibois, A.Ph.A., 57, 1909, 248.

Zinc Phenolsulfonate.—(Manufacture) Lyons, A.J.P., 42, 1870, 508; Takagi and Kutani, C.A., 18, 1924, 1731.

Zinc Stearate.—(Manufacture) Cook and Dosch, Am. Dr., 55, 1909, 105. (Dangers) Anon., Pharm. Era, 56, 1923, 619; Anon., A.J.P., 97, 1925, 496.

Zinc Sulfate.—(History) Arny, Am. Dr., 34, 1901, 3. (Manufacture) Borre, Jl. chim. med., [4], 5, 454, through Gmelin-Kraut, 4^1, 1911, 39; Chemnitius, C.A., 24, 1930, 707.

Lithopone.—Cooper, Jl. Soc. Ch. Ind., 46, 1927, 552; Bannard, *ibid.*, 48, 1929, 335.

Zinc Valerate.—(Manufacture) Brun-Buisson and Lefort, A.J.P., 18, 1846, 243.

Manganese.—(History) Arny, Am. Dr., 34, 1901, 3; Hackh, A.J.P., 90, 1918, 670. (Tests) Dobbin, Jl. Soc. Ch. Ind., 35, 1916, 80. (Manufacture) Procter, A.J.P., 22, 1850, 297. (Therapeutics) Wester, C.A., 22, 1928, 3681; Titus and Cave, Science, 68, 1928, 410; McCollum and Orent, *ibid.*, 73, 1931, 507.

Manganese Bronze.—Corse and Skillman, Met. Ch. Eng., 12, 1915, 113.

Manganese Dioxide.—(Manufacture) Gotthalf, A.J.P., 75, 1903, 214.

Manganese Sulfate.—(Manufacture) Diehl, A.Ph.A., 14, 1866, 249; Livermore, A.J.P., 24, 1852, 9.

Cobalt.—(History) Hackh, A.J.P., 90, 1918, 570. (Production and uses) Mason, C.A., 18, 1924, 809; Gant, Jl. Soc. Ch. Ind., 44, 1925, 157 and 191; Anon., *ibid.*, 50, 1931, 711.

Stellite.—Scoville, Bull. Pharm., 32, 1918, 249; Haynes, Ch. News, 123, 1921, 295; J. Soc. Ch. Ind., 43, 1924, 61; Losee, Jl. Soc. Ch. Ind., 44, 1925, 451T; Drury, C.A., 24, 1930, 5704; Deloro, C.A., 26, 1932, 3464.

Sympathetic Ink.—Vanino, Arch. Pharm., 253, 1915, 505.

Nickel.—(History) Hackh, A.J.P., 90, 1918, 568. (Sources) Anon., Jl. Soc. Ch. Ind., 44, 1925, 892; Anon., Jl. Ind. Eng. Ch., 22, 1930, 806. (Refining and uses) Lathe, Jl. Soc. Ch. Ind., 44, 1925, 433T; Walter, C.A., 25, 1931, 4498.

Ni-chrome.—Anon., Elect. World, 68, 1916, 80.

Smalt.—Duboin, C.A., 15, 1921, 4053.

CHAPTER XXX

ALUMINUM, CERIUM, CHROMIUM, AND URANIUM

In the last chapter (p. 532) it was stated that the third and fourth groups into which the metals are divided in analytic chemistry include all those elements precipitated from alkaline solution by ammonium sulfide.

It was also learned that the third group were those elements whose hydroxides redissolved in excess of ammonium hydroxide; while the hydroxides of the fourth group, aluminum, iron, cerium, and chromium, did not dissolve in ammonia water. These four metals form, even as did the metals discussed in the last chapter, a group that should be included in one chapter. Since, however, the compounds of iron used in medicine are so numerous and valuable, it is deemed best to consider these in a special chapter, leaving aluminum, cerium, and chromium to be discussed in this chapter.

ALUMINUM

Symbol, Al. Atomic weight, approximately 27

Aluminum is one of the most widely distributed of metals, being found in the form of silicate in *clay*, which is one of the most abundant constituents of the earth's crust. A rare and valuable form of the silicate is sodio-aluminum sulfosilicate, the precious mineral, *lapis lazuli*, while among the oxides of aluminum are found several of the most valuable precious stones, such as *ruby* (which, next to diamond, is the hardest of minerals) and *sapphire*. The color of the ruby is due to a trace of chromium, while the sapphire is tinted with cobalt. *Emerald* is a silicate of aluminum and beryllium, with a trace of chromium sesquioxide (Cr_2O_3). *Emery* is a native granular form of aluminum oxide.

While the salts of aluminum, especially alum, have been known from ancient times, the metal was first isolated by Friedrich Wöhler, in 1827, by heating aluminum chloride with metallic potassium in a well-closed crucible.

Wöhler soon found he could obtain the same results by the use of the cheaper metal, sodium. From the time of its isolation by Wöhler, efforts were made to devise a cheap process of manufacture, since its lightness, toughness, and, above all, its disinclination to oxidize—to rust, as iron does—gave promise of its great value in the arts.

Metallic potassium and sodium are costly metals; hence aluminum so separated could never compete, in price, with iron. Experiments in this direction, however, especially those performed under the patronage of Louis Napoleon, while emperor, led to the methods of extraction of the metals sodium and potassium, devised by St. Clair Deville, and a marked reduction in the price of these metals.

Aluminum, one of the most abundant of elements, found in the very rocks and clay beneath our feet, proved one of the most difficult to isolate, and it was not until 1886—over half a century after its first isolation by Wöhler—that a cheap method of obtainining the metal was devised and that in the same year (1886) by an American, C. M. Hall and a Frenchman, P. L. V. Heroult. This method is by electrolysis.

Already, on p. 389, we learned that molten salt, when acted upon by an electric current, is so decomposed that the positive element, sodium, goes to the negative pole, while the negative, chlorine, goes to the positive pole, of the battery. This process Hall and Heroult applied to the separation of aluminum from its oxide, emery, and that on a large scale. The process operates on the same principle as an electric arc light, which is produced by passing a powerful current of electricity through carbon rods representing the positive and negative poles of the battery or dynamo. In the Hall and the Heroult processes a powerful current is run through two bundles of carbon rods several feet long, plunged in a mixture of cryolite and aluminum oxide. The great heat produces a fusion of the mixture and the oxide is then decomposed by the current into the metal. Extra aluminum oxide is added from time to time to make up for that removed as the metal, thus making the process practically continuous. These processes have revolutionized the aluminum industry by bringing the price of the metal to a figure permitting its general use. To Americans, the Hall discovery should be a matter of peculiar satisfaction, inasmuch as through it the center of aluminum production was shifted from Germany and Switzerland to America.

In 1855 a pound of aluminum cost about $125; in 1856 (the St. Clair Deville process of making cheaper sodium having been introduced) the price dropped to about $37 a pound; in 1886, the price was $12.50 a pound; in 1891 (the Hall-Heroult process having been introduced) the price fell to 60 cents a pound. In 1885 the world's output of aluminum was about 26,000 pounds of which 75 per cent was produced in Germany and Switzerland; in 1931, 400,000,000 pounds were produced of which the larger part was of American origin.

As obtains so frequently in the case of important discoveries, Hall's right to distinction as the discoverer of the electrolytic metallurgy of aluminum has been challenged by the adherents of Cowles Brothers, who claim that these gentlemen produced metallic aluminum several years before Hall did.

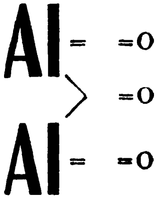
Aluminum is a bright, silvery metal, having the specific gravity of 2.7. It is not easily oxidized, and on account of its comparative toughness and great lightness it was expected to play an important rôle in our metallic industries. Enthusiasts even predicted the eventual substitution of aluminum for iron in much structural work. Experience, however, has not substantiated the claims of the friends of aluminum, it being found that the tensile strength of aluminum is quite low. When warmed, it becomes decidedly brittle. It was also hoped that aluminum would be of considerable service in chemical utensils where platinum must now be used, such as in distillations. This, however, was not borne out by facts. Therefore the chief use of aluminum at the present time is for trinkets and ornaments, and, to a certain extent, for cooking utensils, its lightness rendering them far preferable to those made of iron. It is also a constituent of many valuable alloys, such as aluminum bronze, while almost all fine analytic balances have beams of aluminum.

Magnalium is an alloy of aluminum with 2 to 10 per cent of magnesium, which is very light and also permanent. It is used in aircraft construction. Among the other light aluminum alloys may be mentioned *duralumin*, *aludur*, *lantal*, and *silumin*.

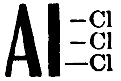
Thermite is a mixture of aluminum oxide and metallic iron, which when heated by burning magnesium, react to form ferric oxide and aluminum with evolution of a great amount of heat, even as high as 3000° C. It is largely used for welding purposes.

Tests.—The tests for aluminum are, first of all, the white precipitate obtained by treating a soluble aluminum salt with ammonium sulfide, the precipitate in this case, however, not being aluminum sulfide, but aluminum hydroxide. A similar precipitate of the flocculent hydroxide is obtained by treating an aluminum salt with any soluble hydroxide. The behavior of this hydroxide with the reagent, however, differs if sodium or potassium hydroxide is used, on the one hand, or ammonium hydroxide, on the other, the precipitate redissolving with an excess of potassium or sodium hydroxide, with the formation of the aluminates of sodium and potassium, $Al(ONa)_3$ or $Al(OK)_3$. The composition of these aluminates is discussed in the chapter on Sodium (p. 485). On the other hand, aluminum hydroxide does not redissolve in an excess of ammonia water.

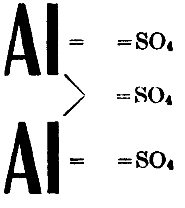
Aluminum is the first metal we have studied having the valence III; hence it is well to consider its combinations. One atom replaces 3 atoms of hydrogen in an acid, as shown by the graphic formulas given below:



Al_2O_3
Aluminum oxide.



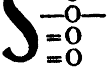
$AlCl_3$
Aluminum chloride.



$Al_2(SO_4)$.

Aluminum sulfate.

It will be noticed in the graphic formula of aluminum sulfate given above that the SO_4 group is represented as attaching itself to the aluminum atom with two bonds. That is, if 2 atoms of hydrogen are removed from H_2SO_4, we have a radical, SO_4, with two free bonds, viz.:



As these two free bonds act exactly as any other free bonds, the SO_4 group in formula writing can be considered exactly as we consider an oxygen atom with its two bonds.

It should be stated in passing that some chemists think that all aluminum compounds contain 2 atoms of that element exhibiting the valence VI, and that the formula of aluminum chloride is not $AlCl_3$, given above, but Al_2Cl_6. This idea is based on the molecular weight estimations, for while $AlCl_3$ would mean molecular weight 133.5, the determinations give figures much nearer 267. The double formula, Al_2Cl_6, is thus explained as is the formula Fe_2Cl_6, which will be considered in the next chapter (p. 558).

The following compounds of aluminum are official:

Alum. Either 99.5 per cent absolute $AlK(SO_4)_2.12H_2O$ or 99.5 per cent $AlNH_4(SO_4)_2.12H_2O$.

Exsiccated alum. Either 96.5 per cent absolute $AlK(SO_4)_2$ or 96.5 per cent absolute $AlNH_4(SO_4)_2$.

ALUMEN—Alum

(Alum.)

$AlNH_4(SO_4)_2.12H_2O$. Ammonium Alum. Molecular weight, 453.32
$AlK(SO_4)_2.12H_2O$. Potassium Alum. Molecular weight, 474.37

Alum contains not less than 99.5 per cent of Ammonium Alum [$AlNH_4(SO_4)_2.12H_2O$] or of Potassium Alum [$AlK(SO_4)_2.12H_2O$]. The label of the container must indicate whether the salt is Ammonium Alum or Potassium Alum.

Summarized Description.

Both forms, in large colorless crystals, in crystalline fragments or as white powder; sweetish, strongly astringent taste; potassium alum is soluble in about 7.2 parts of water, insoluble in alcohol, quite soluble in glycerin; ammonium alum, somewhat less soluble in water than is the potassium compound. For details, see U.S.P., p. 49.

For *tests for identity*, for *impurities* (heavy metals, arsenic, iron, alkalis and alkaline earths) and for *assay*, see U.S.P., p. 50.

Remarks.—It should be noted that the Pharmacopœia recognizes under the name "alumen" either potassa alum, or ammonia alum; the only specification being that each shall be sold under its own name. As to potassa alum, sometimes its formula is written $K_2Al_2(SO_4)_4 + 24H_2O$, while other authorities including the Pharmacopœia give it as $KAl(SO_4)_2 + 12H_2O$.

At first glance, the symbolic formula, $K_2Al_2(SO_4)_4 + 24H_2O$, seems exceedingly complicated, but viewed in the light of the synonym—aluminum and potassium sulfate—it becomes simplified. What is aluminum sulfate? We have just learned above that it is $Al_2(SO_4)_3$. And potassium sulfate? This is derived from sulfuric acid, H_2SO_4, by replacing its two hydrogen atoms with 2 atoms of the univalent element, potassium:

Hence, K_2SO_4,
If we add to this aluminum sulfate, $Al_2(SO_4)_3$,
We get $Al_2K_2(SO_4)_4$,

and if we crystallize this with 24 molecules of water of crystallization, we have the formula $K_2Al_2(SO_4)_4 + 24H_2O$.

The reason that this is not written $Al_2(SO_4)_3K_2SO_4 + 24H_2O$ is because the union between the sulfate of aluminum and potassium is stronger than a mere physical mixture. We believe that there exists between the two salts a chemical relationship, somewhat akin to that between a salt and its water of crystallization.

Ammonia alum was the "alumen" of the Pharmacopœia of 1870, but was replaced in the Pharmacopœia of 1880 by the potassa alum. It is now used as frequently as potassa alum since the cost of the two is about the same.

Let us compare the formula of these two alums, representing them as broken into the sulfates of the two metals:

Potassium alum is.... ... . $K_2SO_4Al_2(SO_4)_3 + 24H_2O$.
Ammonium alum is.................... $(NH_4)_2SO_4Al_2(SO_4)_3 + 24H_2O$.

The only difference between these two is that in one we have potassium sulfate; in the other, we find ammonium sulfate, each being combined with aluminum sulfate and with 24 molecules of water of crystallization.

When we closely consider the two formulas just given, we find that each represents 1 molecule of the sulfate of a univalent element, 1 molecule of a sulfate of a trivalent element, and 24 molecules of water of crystallization. We have seen that the univalent element or radical can be changed; for in the two alums just mentioned one contained potassium sulfate, the other ammonium sulfate. In like manner we can make a sodium alum of the formula $Na_2SO_4Al_2(SO_4)_3 + 24H_2O$. We have changed the univalent element or radical three times. Can we thus change the trivalent element? Most assuredly, replacing aluminum by the trivalent elements, iron, manganese, or chromium, getting such compounds as:

$K_2SO_4Al_2(SO_4)_3 + 24H_2O$	Potassium alum.
$K_2SO_4Fe_2(SO_4)_3 + 24H_2O$	“ ferric alum.
$K_2SO_4Mn_2(SO_4)_3 + 24H_2O$	“ manganese alum.
$K_2SO_4Cr_2(SO_4)_3 + 24H_2O$	“ chromium alum.
$(NH_4)_2SO_4Al_2(SO_4)_3 + 24H_2O$	Ammonium alum.
$(NH_4)_2SO_4Fe_2(SO_4)_3 + 24H_2O$	“ ferric alum.

We see how many alums can be produced; hence the only general definition of an alum that can be given is that mentioned above: "the combination of 1 molecule of the sulfate of a univalent element or radical, with 1 molecule of the sulfate of a trivalent element or radical, and with 24 molecules of water of crystallization." Not only do all alums crystallize with the same proportion of water, but also their crystal shapes are the same—in other words, they are *isomorphous*.

Alum has been made for centuries from certain ores of aluminum, particularly alum shale. This is a form of clay containing iron pyrites (FeS_2), and on letting the ore stand exposed to the elements for one to two years, the ferric sulfide is changed to ferrous sulfate, ferric subsulfate, and free sulfuric acid, and the latter in turn reacts with the clay (aluminum silicate) to form aluminum sulfate. Roasting the ore after standing effects the liberation of more sulfuric acid from the iron sulfates, and the roasted mass on lixiviation yields a solution of aluminum sulfate contaminated with more or less iron. Various methods are employed in removing the iron, such as long standing of the solution exposed to the air, when the iron precipitates as ferric oxide; placing pieces of iron in the solution, which converts all the dissolved iron into ferrous sulfate, which is separated from the aluminum sulfate by fractional crystallization.

The concentrated and pure aluminum sulfate solution is then mixed with potassium (or ammonium) chloride or sulfate, and at the proper degree of concentration crystals of alum begin to separate.

Potassium chloride is used because more abundant than potassium sulfate, and when mixed with aluminum sulfate solution, yields a double sulfate of potassium and aluminum, as shown in the following equation:

$$4Al_2(SO_4)_3 + 6KCl = 3K_2Al_2(SO_4)_4 + Al_2Cl_6.$$

Alum is also made on a large scale from the aluminum hydroxide, which is a side product in the cryolite process (p. 485). Alum occurs in large crystals soluble in 7.2 parts of water and freely soluble in glycerin. It is a curious fact that from a saturated aqueous solution, the alum crystallizes when glycerin is added and likewise crystallization occurs when water is added to a saturated glycerinic solution.

Alum is used as an astringent, either internally or else externally in the form of a wash. It is also used as a styptic, to staunch the flow of blood from a wound, but Hanzlik does not find it as effective as other substances.

ALUMEN EXSICCATUM—Exsiccated Alum

(**Alum. Exsic.**—Dried Alum, Burnt Alum)

Exsiccated Alum, when recently dried to constant weight at 200° C., contains not less than 96.5 per cent of Ammonium Alum [$AlNH_4(SO_4)_2$] or of Potassium Alum [$AlK(SO_4)_2$].

The label of the container must indicate whether the Exsiccated Alum was made from Ammonium Alum or Potassium Alum.

Storage.—Preserve in air-tight containers.

Summarized Description.

White, odorless powder; sweetish astringent taste; soluble in about 20 parts of water; insoluble in alcohol. For details, see U.S.P., p. 50.

For *tests for identity* and for *impurities*, see alum. For *assay*, see U.S.P., p. 50.

Remarks.—This official is obtained by the exsiccation of crystallized alum, 100 parts of the crystal yielding 55 parts of the dried alum. (See p. 175.)

Exsiccated alum is used as a mild escharotic under the name of *burnt alum*, being particularly efficacious for the removal of that form of morbid growth developing in an open sore called proud flesh.

Alumini Hydroxidum (U.S.P. IX) or *Aluminum Hydroxide*, $Al(OH)_3$, is made by adding a solution of alum to a solution of sodium carbonate. This may at first produce aluminum carbonate, but if such is the case, it is only for an instant, the carbonate decomposing with the evolution of carbon dioxide, forming a precipitate of aluminum hydroxide. In preparing aluminum hydroxide it is important that the alum solution be added to the sodium carbonate solution, and not the reverse method, as in the latter case the hydroxide will be contaminated with alkaline sulfates.

A point of importance in the manufacture of chemicals by precipitation is this very question of which chemical solution should be added to the other. The pharmacist, therefore, should carefully consult the best authorities before attempting such a precipitation, as it frequently happens that while the product yielded by one method is perfectly pure, that yielded by the reverse process is practically worthless.

One of the most interesting things in connection with aluminum hydroxide is its vast capacity for water, a fresh, well-drained magma of aluminum hydroxide containing no less than 95 per cent of water.

Aluminum hydroxide is a white, bulky, amorphous powder, insoluble in water but soluble in diluted acids and in alkaline hydroxide solutions. It is a valuable absorbent, and therefore useful in dusting powders.

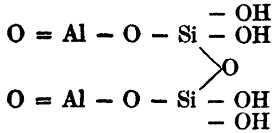
Aluminum Acetate, $Al(C_2H_3O_2)_3$, is an easily decomposable salt that can be prepared by treating aluminum hydroxide with acetic acid. *Solution of aluminum subacetate* (N.F. VI) is prepared by dissolving aluminum sulfate in water, adding precipitated chalk and acetic acid and finally separating the clear fluid from the magma. It contains about 8 per cent of basic aluminum acetate (p. 213).

Liquor Alumini Acetatis (N.F. VI), or *Burow's Solution*, is made by mixing solutions of lead acetate and of aluminum sulfate and finally separating the clear fluid from the magma of lead sulfate. (See p. 213.)

Alumini Sulfas (N.F. VI) or *Aluminum Sulfate*, $Al_2(SO_4)_3 + 16H_2O$, is prepared by dissolving moist aluminum hydroxide in diluted sulfuric acid, and then granulating the salt by evaporation of the solution.

Aluminum sulfate is used internally as an antiseptic, but chiefly externally as an astringent. Its astringent properties make it of great value as a fixer in dyeing.

Kaolinum (N.F. VI) or *Kaolin*, $Al_2Si_2O_9H_4$, is an aluminum silicate the structural formula of which is still a matter of dispute. While Mellor and Holdcroft originally thought the formula was:



they are now inclined to the belief that it is much more complex. Kaolin is found in various parts of the world including Colorado and is of great value in technic as a basis of porcelain. A description of the manufacture of porcelain is beyond the limits of this work, and for this the reader is referred to any of the leading works on chemical technology mentioned in the Preface. Kaolin is of pharmaceutic importance as having been suggested for use in the manufacture of the pills of potassium permanganate and other explosive substances, these substances being mixed with kaolin and made into a mass by the addition of soft petrolatum. Kaolin is now largely used in the form of poultice, made by triturating the finely powdered clay with glycerin to a thick paste. A similar product is *cataplasm of kaolin*, N.F. (See p. 374.)

It possesses marked adsorbent (see p. 156) properties and is now used in medicine as an adsorbent of intestinal bacteria.

Fuller's Earth is another type of clay, not identical with kaolin, largely used as a clarifier of oils. A specially purified type now known as *Lloyd's Reagent* possesses adsorbent properties to such a remarkable degree that it is used to remove alkaloids from their solutions, the adsorbed alkaloid remaining in the silicate in easily assimilable form.

Bentonite is a colloidal form of soda clay mined in Canada and the United States. It adsorbs 10 times its own weight of water and is now used largely as textile "filler." Bentonite "gel" is used as the basic of "beauty clays" so largely used as cosmetics.

Bear in mind that two other absorbent earths are frequently employed: *talc* (p. 519) and *purified siliceous earth* (p. 437).

Ultramarine is a blue pigment made originally by pulverizing the mineral lapis lazuli. Analysis showing that this consists of silicates of aluminum and sodium combined with sulfur; its artificial production has been followed with much success. It is used to whiten sugar.

CERIUM

Symbol, Ce. Atomic weight, approximately 140

Cerium is a rare metal, similar in many respects to aluminum. It is of technical importance because the "mantle" of the Welsbach burner —that well-known mode of illumination—is made of a network of oxides of cerium, thorium, didymium, and lanthanum, the last two elements usually accompanying cerium in its ores.

The sole pharmaceutic interest in cerium is because one of its salts, the oxalate, was recognized by former Pharmacopœias.

Cerii Oxalas (U.S.P. IX; N.F. VI) or *Cerium Oxalate*, $Ce_2(C_2O_4)_3$, is not the true oxalate but a mixture of it with didymium and lanthanum oxalates. It is a white or slightly pink powder that is insoluble in water. It is considered of much value in the vomiting of pregnancy. *Dose.*—200 mg. (3 grains).

CHROMIUM

Symbol, Cr. Atomic weight, approximately 52

Chromium, like manganese, aluminum, zinc, and iron, stands midway between the positive and negative elements, forming chromium salts, such as chromous sulfate, $CrSO_4$, with strong acids; and chromates, such as potassium chromate, K_2CrO_4, with alkalis.

However, it is usually more negative than positive, and in its official compound, chromium trioxide, it is distinctly negative.

The chief ore of chromium is chrome iron ore, $FeOCr_3O_3$, half of which is now obtained from Rhodesia, South Africa. (See p. 474.)

The word chromium is derived from the Greek word *chromos*, meaning color, and is so called by reason of the brilliant characteristic color of the various chromium compounds. This name was bestowed on the element by its discoverer, Vauquelin.

The element chromium is isolated either by the reduction of chromic oxide with soot or coke, or, better, by fusion of a mixture of the chlorides of chromium, potassium, and sodium with zinc. The alkaline chlorides act as a flux, while an alloy of zinc and chromium deposits in the bottom of the crucible. This alloy is treated with diluted nitric acid, which dissolves the zinc, leaving chromium as a gray powder.

Chromium is a gray-white, brittle metal, hard enough to scratch glass, and more difficult to melt than platinum. It is not easily oxidized by contact with air.

It is now used in the manufacture of *stainless steel*, which is an alloy containing about 85 per cent of iron, 14 per cent of chromium, and 0.1 per cent of carbon.

During the past decade, the art of chromium electro-plating has been perfected and the products are now used enormously for decorating buildings.

The characteristic tests of chromium are as follows:

Ammonium sulfide precipitates, from the solution of chromium compounds, green chromic hydroxide, potassium hydroxide producing the same precipitate; lead acetate solution precipitates solutions of chromium compounds in the form of a yellow lead chromate (chrome yellow), which is rather largely esteemed as a paint. It should not, however, be used in coloring buns in place of the yolk of egg, as was tried by the bakers of Philadelphia some forty years ago, with disastrous results.

Chromium yields several oxides—chromium oxide, CrO; chromium tetroxide, Cr_3O_4; chromic oxide, Cr_2O_3; chromium dioxide, CrO_2; chromium trioxide, CrO_3. The variation in valence represented by these oxides leads to considerable confusion, and for this reason the element chromium was omitted from the table of elements on p. 390. A similar confusion is encountered in the naming of its oxides, it being particularly unfortunate that the term "chromic oxide" is applied to Cr_2O_3. We have been taught that an "ic" oxide should yield the corresponding "ic" acid, and yet the official formerly called "chromic acid" is not derived from Cr_2O_3, but is none other than chromic trioxide, mentioned above.

CHROMII TRIOXIDUM—Chromium Trioxide

(Chrom. Triox.—Chromic Anhydride)

CrO_3. Molecular weight, 100.01

Chromium Trioxide contains not less than 95 per cent of CrO_3.

Caution.—Chromium trioxide should not be brought into intimate contact with organic substances, as serious explosions are likely to result.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

Small, purplish-red, needle-shape crystals or rhombic prisms; destructive to animal or vegetable tissues; deliquescent; soluble in about 0.6 part of water; decomposes (sometimes with explosions) in alcohol and other organic solvents; on heating, darkens, then fuses, then dissociates with oxygen and other chromium oxides. For details, see U.S.P., p. 120.

For *tests for identity*, for *impurities* (sulfuric acid) and for *assay*, see U.S.P., p. 120.

Remarks.—This compound has the formula CrO_3. In this, as in sulfuric oxide, SO_3, the valence of the characteristic element is VI. It will be seen that this so-called "acid" is in reality an oxide; the true acid (the formula of which is H_2CrO_4, and thus similar to that of sulfuric acid, H_2SO_4) existing only in solution.

Wyrouboff thinks that the chromic acid found in aqueous solution is really $H_2Cr_2O_7$.

The official is, therefore, the anhydride of true chromic acid; an anhydride of an acid being an acid deprived of what water it possessed in the form of hydroxyl groups. This is the first acid anhydride which we have studied that is commonly given the name of the acid; the other official one being arsenous acid. In both cases they are called acids instead of oxides because they are the nearest approach to the true acid which can be obtained in the solid form, and, moreover, on dissolving these oxides in water, the true acid is produced.

Chromic acid is made by treating the potassium dichromate with a molecular quantity of sulfuric acid by the following reaction:

$$K_2Cr_2O_7 + 2H_2SO_4 = 2CrO_3 + 2KHSO_4 + H_2O.$$

It will be seen, from the equation, that enough sulfuric acid is used to convert the potassium into potassium bisulfate. This salt is removed by crystallization, and the mother liquid then further concentrated, when the crop of chromic acid crystals is produced. These crystals cannot be dried as in ordinary cases by placing on bibulous paper, since chromium trioxide is a very powerful oxidizing agent, and will decompose most organic substances, including paper. Therefore, instead of paper, some inorganic absorbing surface must be used. For this purpose unglazed porcelain or clean fire-brick is excellent. If the use of either of these is inconvenient, drying plates of plaster of paris can be used with excellent results. Such plates are made by making a fairly thick paste of plaster of paris in water, and allowing same to set in an appropriate mold, for example, the cover of a pasteboard box—and after thoroughly drying the porous plate is obtained.

By reason of the oxidizing action of the chromic acid the Pharmacopœia sounds a note of warning against triturating this chemical with easily oxidizable material. Hence beware of prescriptions directing chromic acid dispensed in pills. These must not be made with ordinary excipient, but with petroleum mass (kaolin and soft petrolatum). The oxidizing action of chromic acid is used for the cleaning of mortars, as already explained on p. 136. Chromic acid is also very largely used in oxidation processes in organic chemistry, for such purposes where nitric acid would act too powerfully. Medicinally, chromic acid is used almost entirely as a caustic, and its use in this way is usually limited to the removal of corns or warts. For this purpose it is very effective, but it should be applied only by a skilled operator, as careless handling of the chemical in such cases is apt to result in dangerous wounds.

Chromium Sulfate, $Cr_2(SO_4)_3$, is made by treating chromic hydroxide with sulfuric acid. It occurs in dark-green scales, soluble in water, and is used in neurasthenia and in prostatic troubles in 4-grain doses.

Potassium Dichromas (U.S.P. VIII) or *Potassium Dichromate*, $K_2Cr_2O_7$, has already been discussed under the potassium compounds, and here it is only necessary to state that it is used chiefly as an oxidizing agent, and for this purpose is used with sulfuric acid, thus liberating chromic acid.

URANIUM

Symbol, U. Atomic weight, 238.2

Uranium is one of the rarer metals whose chief ore, *pitchblende*, has recently come into prominence as the source of radium. Like radium salts, those of uranium exhibit radio-activity. One uranium salt was recognized in the former Pharmacopœia.

Uranii Nitras (U.S.P. IX) or *Uranium Nitrate*, $UO_2(NO_3)_2$, is a salt in which uranium exhibits the valence VI. It is made by dissolving uranium oxide, UO_3, in diluted nitric acid and crystallizing the resulting fluid.

It occurs in light yellow prisms, is radio-active and is quite soluble in water, alcohol, and ether. It is used (with caution) in diabetes. *Dose.*—10 mg. (1/6 grain).

BIBLIOGRAPHY

Aluminum.—(History) Deville, Dr. Circ., 13, 1869, 102; Hall, J. Ind. Eng. Ch., 3, 1911, 143; Saunders and McMillin, Jl. Ind. Eng. Ch., 8, 1916, 474; Matignon and Faurholt, C.A., 19, 1925, 1212; Van Doren, Jl. Ind. Eng. Ch., 21, 1929, 120; Holmes, Jl. Ch. Ed., 7, 1930, 233; Science, 83, 1936, 174. (Metallurgy) Hall, *ibid.*, 3, 1911, 143; Anon., C.A., 12, 1918, 1150. (Production) Richards, C.A., 14, 1920, 2905; Anon., C.A., 22, 1928, 195; Edit., Jl. Soc. Ch. Ind., 48, 1929, 309; Gregory, *ibid.*, 50, 1931, 390. (Therapeutics) Thieme, Jl. Soc. Ch. Ind., 49, 1930, 263B; Burn, Analyst, 57, 1932, 428; Weidlein and Beal, Mellon Inst. Bib. Series No. 3, 1933, 1–69.

Magnalium and Other Light Alloys.—Anon., C.A., 5, 1911, 451; Schultz, C.A., 18, 1924, 2676; Bossert, Jl. Soc. Ch. Ind., 48, 1929, 983B; Vogel, C.A., 23, 1929, 5145; Harvey, C.A., 23, 1929, 5145 and 24, 1930, 578.

Thermite.—Duncan, Chemistry of Commerce, 1907, 90.

Aluminum Chloride.—(Formula) Friedel and Craft, A.Ph.A., 37, 1889, 547; Nilson and Peterson, Zt. phys. Ch., 4, 1889, 206. (Manufacture) McAfee, Jl. Soc. Ch. Ind., 48, 1929, 836.

Solution of Aluminum Acetate.—Liebig, A., 74, 1850, 193; Schmatolla, C.A., 26, 1932, 3618; Freitag, Jl. Soc. Ch. Ind., 44, 1925, 336B.

Solution of Aluminum Subacetate.—Arny, Pract. Dr., 41, July, 1923, 20.

Burow's Solution.—Raubenheimer, A.Ph A., 57, 1909, 1036.

Aluminum Hydroxide.—(Composition) Martin, C.A., 10, 1916, 571. (Properties) Zsigmondy, C.A., 20, 1926, 2266; Robinson and Britton, Jl. Ch. Soc., 120, 1931, 2817; Kohlschütter and co-workers, C.A., 26, 1932, 1492. (Therapeutics) Crohn, C.A., 24, 1930, 3561.

Alums.—(Composition) Parsons and Evans, Jl. Am. Ch. Soc., 32, 1910, 1378. (Sodium alum) Smith, Jl. Am. Ch. Soc., 31, 1909, 245; Leffmann and Strock, C.A., 22, 1928, 2522.

Alum, U.S.P.—(History and manufacture) Bell, Ch. News, 12, 1865, 221, 234 and 265; Patterson, Jl. Ind. Eng. Ch., 18, 1926, 634; Nicol, Jl. Soc. Ch. Ind., 52, 1933, 156. (Solubility) Dunlop, Ph. Jl., 85, 1910, 6. (Medical uses) Hanzlik, Jl. A.M.A., 72, 1919, 577.

Kaolin.—(Formula) Mellor and Holdcroft, C.A., 5, 1911, 2537 and 8, 1914, 1102; Rohland, C.A., 8, 1914, 2042; Samoilov, C.A., 8, 1914, 3767; Isobe and Watanabe, C.A., 26, 1932, 565; Seto, C.A., 24, 1930, 1059. (Sources) Anon., Am. Dr., 19, 1890, 147; Keenan, Am. Dr., 62, 1914, 31; Anon., Ph. Jl., 128, 1932, 165. (Properties) Rohland, C.A., 8, 1914, 1102; Ginzburg, C.A., 9, 1915, 578; Keppeler, C.A., 24, 1930, 4976; Wiegner, Jl. Soc. Ch. Ind., 50, 1931, 103T; Noll, C.A., 26, 1932, 4686. (Medical uses) Lowe, A.J.P., 92, 1920, 230; Walker, C.A., 15, 1921, 3327; Anon., A.J.P., 98, 1926, 369.

Fuller's Earth.—(Source) Miser, C.A., 6, 1912, 3255; Vollertsen, C.A., 13, 1919, 3287; Maynard and Mallon, Ch. Met. Eng., 26, 1922, 1074; Deckert, C.A., 20, 1926, 802. (Synonyms) Anon., A.J.P., 102, 1930, 45. (Adsorptive power) Seidell, Jl. Am. Ch. Soc., 40, 1918, 312; Rideal and Thomas, C.A., 17, 1923, 15; Benedict, C.A., 20, 1926, 2084; Eckart, Jl. Soc. Ch. Ind., 45, 1926, 448B; Davidsohn, C.A., 22, 1928, 3310; Heller, C.A., 23, 1929, 3823; Phelps, C.A., 25, 1931, 4457. (Lloyd's reagent) Lloyd, Jl. A.Ph.A., 5, 1916, 381; Rehfeld, Jl. A.Ph.A., 3, 1914, 710; Gordin and Kaplan, *ibid.*, 3, 1914, 627; Fantus, Jl. A.M.A., 64, 1915, 1838 and Jl. A.Ph.A., 4, 1915, 826; Jensen, Ph. Jl., 105, 1920, 97.

Bentonite.—(Sources and Properties) Alexander, Jl. Ind. Eng. Ch., 16, 1924, 1140; Spence, C.A., 19, 1925, 628; Woodman and Taylor, Jl. Soc. Ch. Ind., 49, 1929, 121T; Davis and Vacher, C.A., 23, 1929, 1843. (Uses) Anon., Jl. Frank. Inst., 207, 1929, 273.

Ultramarine.—Hoffmann, Ch. Zt., 34, 1910; 821; Kalshoven, C.A., 13, 1919, 2767; Bock, Jl. Soc. Ch. Ind., 39, 1920, 306A; May, Jl. Soc. Ch. Ind., 43, 1924, 83; Violet, C.A., 20, 1926, 3241; Leschewski and Möller, C.A., 26, 1932, 2065.

Cerium.—(History) Hackh, A.J.P., 90, 1918, 573. (Sources) Santmyers, C.A., 24, 1930, 5004. (Isolation) Kremers and Beuker, Jl. Soc. Ch. Ind., 44, 1925, 407B; Billy and Trombe, C.A., 25, 1931, 5858. (Properties) Lortie, C.A., 25, 1931, 1750. (Medical uses) Koch, Jl. A.M.A., 75, 1920, 246; Hara, C.A., 18, 1924, 1340.

Cerium Oxalate.—Mayer, A.J.P., 32, 1860, 1; Pomer and Shedden, Jl. Soc. Ch. Ind., 19, 1900, 636; Gane and Webster, Drug Topics, 20, 1905, 211.

Welsbach Mantles.—Heger, Am. Dr., 15, 1886, 49; Duncan, The Chemistry of Commerce, 1907, 72.

Chromium.—(History) Vauquelin, Ann. chim., 1798 and 1809, through Gmelin-Kraut, 3, 1911, 311. (Production) Anon., Jl. Soc. Ch. Ind., 42, 1923, 857; Anon., Science, 64, Aug. 6, 1924, xiv; Smith, Bureau of Mines Inf. Circ. 6566, 1932, 1–36. (Properties) Hoffmann and Tingwaldt, C.A., 25, 1931, 5326. (Chromium plating) Ollard, Jl. Soc. Ch. Ind., 44, 1925, 888; Schneidewind, 23, 1929, 775; Dobbs, Jl. Soc. Ch. Ind., 49, 1930, 161T; Kaspar, C.A., 26, 1932, 5852; Blum, Jl. Frank. Inst., 213, 1932, 17; Hentschel, C.A., 26, 1932, 1196.

Stainless Steel.—Becket, Ch. Met. Eng., 30, 1924, 317; Anon., Jl. Soc. Ch. Ind., 52, 1932, 49; Kawakami, Jl. A.Ph.A., 18, 1929, 737.

Chrome Yellow.—(Composition) Groeger, C.A., 14, 1920, 2450. (Poison) Harrington, Dr. Circ., 31, 1887, 46.

Chromium Trioxide.—(Manufacture) Bolley, A.J.P., 18, 1847, 199. (Explosive character) Anon., A.Ph.A., 23, 1875, 296. (Oxidizer) Anon., A.Ph.A., 31, 1883, 200.

Chromic Acid.—Wyrouboff, C.A., 8, 1914, 1037; Datta and Dhar, Jl. Am. Ch. Soc., 38, 1916, 1303.

Chromium Sulfate.—Ross, Dr. Circ., 54, 1910, 274; Senechal, C.A., 8, 1914, 3539.

Uranium Nitrate.—Buchholz, Gmelin-Kraut, 3^1, 1912, 1080.

CHAPTER XXXI

IRON

Symbol, Fe. Atomic weight, approximately 56

THE most useful and abundant of metals is *iron.* Its use is so diversified, both technically and pharmaceutically, that we must give it careful consideration.

The element is widely distributed on the earth, but in no place as the pure metal. It oxidizes (rusts) so rapidly that it cannot long remain pure in the earth's atmosphere. We find pure native iron only in the interior of meteoric stones which fall from the heavens, and are supposedly fragments of the sun's substance. This leads to the conclusion that the sun's atmosphere must be composed of some gases other than oxygen.

The principal ores of iron found on the earth's surface are as follows: *Magnetic iron ore* or *lode stone.* This ore, the history of which has been discussed on p. 540, has the formula Fe_3O_4, and is supposed to be a ferrous ferrate, $Fe(FeO_2)_2$, being derived from a hypothetic acid, $HFeO_2$, which is analogous to the aluminum compound already described on p. 485.

The name ferric acid is not applied to this compound, however, as it appears that there is an acid, H_2FeO_4, in which iron shows the valence VI.

The potassium salt of this acid, K_2FeO_4, is known.

This magnetic iron ore is used more by reason of its magnetic properties than as a source of iron. The commercial ores are chiefly *red hematite*, Fe_2O_3, *spathic iron ore*, $FeCO_3$, and *iron pyrites*, FeS_2. This last has already been discussed on p. 449 as one of the sources of sulfuric acid, so here it need only be stated that the term "pyrites" is derived from the Greek word *pyros*, fire, and is used in this case because, when the ore is struck, it emits sparks. Iron pyrites is also interesting as being the only iron compound in which iron shows the valence IV. Besides these commercial sources of iron, references should be made to the fact that this element is found in chlorophyll and in the blood, and in both cases its presence is necessary to the life of both plant and animal. So soon as the chlorophyll of the plant or the hematin of the blood becomes deficient in iron, the assimilation processes of the plant or animal economy lessens, with corresponding disastrous results to the organism. When iron is absent from the chlorophyll of plants or from the blood corpuscles, such plants or animals are said to be anemic.

Iron has been known from ancient times as one of the most valuable of metals. In fact, one of the most important steps in the development and progress of humanity is known by ethnologists and archeologists as the transition from the stone to the iron age.

VARIETIES OF IRON

The commercial forms of the metal iron can be roughly divided into three groups—cast iron, steel, and wrought iron. The difference between these three groups is based on the amount of carbon contained in the metal. Thus, *cast iron* contains from 3 to 6 per cent carbon; *steel*, from 0.8 to 1.8 per cent of carbon; and *wrought iron*, from 0.2 to 0.6 per cent carbon.

The origin of these different varieties of iron is merely a question of the manipulation. Cast iron is prepared by treating the ore (an oxide of iron) with coke and limestone in the presence of a blast of air. The coal in this case acts as a reducing agent, as shown in the following equation:

$$Fe_2O_3 + C_3 = Fe_2 + 3CO.$$

The carbon monoxide produced also acts as a reducing agent on the ore, ultimately escaping as carbon dioxide (CO_2). The function of the limestone is to form a combination with the silicates naturally found in ore, the resulting calcium silicate separating in the form of *slag*, which floats on the surface of the molten iron. This process goes on in a special apparatus (blast furnace) lined with brick or fire clay, and it is so arranged that the process is continuous; alternate layers of the ore, coal, and limestone being dumped in at the top, meeting the fiery blast produced by combustion of the preceding portions of coal about midway down in the apparatus, and molten iron drawn from the bottom.

Wrought iron is prepared by removing all the carbon from the cast iron by keeping the latter in the molten state for a time sufficient to burn the carbon contained therein by contact with the air. There are two general methods of accomplishing this result: first and oldest is called puddling, and consists of melting the cast iron in flat vessels lined with hematite having considerable surface exposed to the air, and stirring same vigorously with an appropriate steel paddle until all the carbon has combined with the oxygen of the air. In the more modern method the molten cast iron is submitted to the action of an air blast, being constantly stirred all the while.

Steel, as will be noted above, contains a carbon percentage midway between that of cast iron and wrought iron. Hence, by the proper blending of these two forms of iron, a steel of any carbon percentage can be obtained, the calculation in this case being by the process of alligation, similar to that already described on p. 73.

This blending is performed by the Bessemer process, the operation being carried on in a special apparatus called the Bessemer converter, consisting of a huge, pear-shaped vessel, lined with fire brick, revolving on a pivot in such a way that it can be inverted. Into this converter the molten cast iron is poured, a blast of air passed therein until the cast iron is converted into wrought iron. The wrought iron is then blended with sufficient cast iron to make a finished product of exactly the carbon content desired. Besides the Bessemer method, steel is now made largely by the open-hearth process. Crucible steel is the name given special types of steel made in high black-lead crucibles and now the Heroult furnace is used for preparing such steels. It is needless to say that this explanation of the manufacture of the three forms of iron is superficial, extended comment thereon being beyond the limits of this volume, and for full details of the process the reader is referred to the articles mentioned in the bibliography at the end of this chapter.

It might, however, be stated that, for the modern manufacture of steel, many recipes are employed, and each modification is usually the secret of the individual ironmaster. Thus, in making these special steels many of the rarer elements, such as uranium and vanadium, are added to impart the desired toughness to the steel.

Several alloys of iron are worth passing notice.

Silicon iron is marketed under such trade names as *duriron* and *tantiron*, the latter containing about 85 per cent of iron and 15 per cent of silicon. Such silicon irons exhibit a marked resistance to acids, it being possible to distil even nitric acid from retorts made of this alloy.

Stainless steel is an iron alloy containing 12 to 14 per cent of chromium. As the name indicates it is not stained by acids and is therefore used for cutlery.

Elinvar is an alloy containing about 33 per cent of nickel, 4 per cent of chromium, 2 per cent of tungsten, 2 per cent of manganese, and 59 per cent of iron. It is used in making nonmagnetic watch springs.

A special type of stainless steel, *"austenitic" ni-chrom steel*, containing about 18 per cent of chromium and 8 per cent of nickel has been found highly resistant to the action of nitric acid and of gaseous ammonia.

Invar is a nickel steel which has practically no coefficient of expansion. It is used for surveying tape and for pendulums.

One modification of steel manufacture is worthy of passing notice. A great drawback in the manufacture of steel from the iron ore obtained in continental Europe was due to the fact that this ore contained a considerable amount of phosphorus, which caused the finished steel to be brittle, and hence comparatively useless. A remedy for this condition was discovered by Thomas and Gilchrist, who employed the simple method of lining the Bessemer converter with calcined dolomite. When the phosphorus-bearing ores were converted into wrought iron in such converters, the phosphorus was absorbed by the calcium and magnesium of the dolomite lining, with the formation of the phosphates of these two metals. Not only does this process afford a ready means of removing the phosphorus from the ore, but the dolomite lining is thereby converted into calcium and magnesium phosphates, having ready sale as a fertilizer.

The properties of iron must be discussed under the three diversified forms just described. All three forms of iron—cast iron, steel, and wrought iron—act chemically as iron, all dissolving in acids to form ferrous, and eventually ferric, salts. Another point showing their iron origin is the fact that all, when exposed to the moist atmosphere, oxidize with the formation of Fe_2O_3, which is familiar to all under the name of *iron rust.* Physically, the three forms show a marked dissimilarity. *Cast iron*, for example, melts at 1150° C., is quite brittle, and hence breaks when hammered. This variety is called cast iron because it shares with water and with bismuth the property of expanding at the moment of solidification. *Steel* melts at 1400° C., and is the reverse of brittle, being, when properly tempered, the most elastic of metals. It is very hard, and hence it is but slightly affected by the blows of a hammer, not breaking as cast iron does, and not flattening as does wrought iron. *Wrought iron* melts at 1500° C. and is neither brittle nor elastic, but is very malleable. In fact, a commercial term for this form of iron is *malleable iron*, and to this property is due its use in the arts.

The steel and iron industry is one of the greatest manufacturing enterprises. Of the 215,000,000 tons of iron and steel produced throughout the world in 1929, 99,000,000 tons were produced in the United States.

There are now so many commercial varieties of metallic iron that the line of demarcation between cast iron, steel and wrought iron, is difficult to draw. Richards suggests that all malleable irons and steels containing less than 2 per cent of carbon be called steel and that all nonmalleable irons be designated as cast iron.

Of the commercial forms of iron just mentioned, wrought iron is the nearest approach to the pure element; steel and cast iron being now considered as mixtures of iron with varying proportions of iron carbide.

Tests.—The tests for iron and its salts are as follows: the black precipitate obtained by treating its solution with ammonium sulfide; the reddish-brown magma by treatment of ferric solutions with ammonium hydroxide, this precipitate being formerly official under the name of *ferri oxidum hydratum;* and the black coloration produced on treating an iron solution with tannin. This latter mixture, when combined with appropriate adhesive agents, forms the typical *black ink*, and is of pharmaceutic interest because such black coloration is produced whenever an iron salt is combined with the preparation of a drug containing tannin.

Besides these tests, far more characteristic are potassium fer*ri*cyanide, which gives a blue precipitate with fer*rous* salts, and potassium fer*ro*cyanide, which gives a blue precipitate with fer*ric* salts. An exceedingly delicate test for ferric salts is the red color produced by potassium thiocyanate.

In former Pharmacopœias three metals, zinc, iron, and mercury, were recognized in their metallic state. In U.S.P. X, the monograph on zinc was dropped and only two metals, iron and mercury, are official; unless we are willing to stretch a point and state that the colloidal silver preparations (p. 626) represent elemental silver. Iron is recognized by the Pharmacopœia in two forms, namely, *ferrum* and *ferrum reductum.*

FERRUM—Iron

(Ferr.)

Symbol, Fe. Atomic weight, 55.84

Elementary Iron (Fe) in the form of fine, bright wire, filings or powder.

Remarks.—This is wrought iron, usually in the form of fine, bright, nonelastic wire, and a popular variety of this is what is commercially termed *card-teeth,* consisting of small points of iron wire used as the teeth of appliances employed in carding wool and cotton.

In dissolving card-teeth in acids, hydrogen is evolved, as shown in the following equation:

$$Fe + H_2SO_4 = FeSO_4 + H_2,$$

but at the same time it will be noticed that a peculiar odor is emitted. This odor is due to the hydrocarbon produced by the combination of the hydrogen with the carbon contained in the card-teeth.

Iron wire is recognized by the Pharmacopœia only as a source of iron compounds, it being the most convenient form from which to make the salts of the metal.

FERRUM REDUCTUM—Reduced Iron

(Ferr. Reduct.—Iron by Hydrogen)

Reduced Iron is obtained by the action of hydrogen upon ferric oxide and contains not less than 90 per cent of metallic iron (Fe).

Storage.—Preserve in well-closed containers.

Summarized Description.

Very fine, grayish-black, lusterless amorphous powder; all must pass through a No. 100 sieve; insoluble in water or alcohol; ignites on heating, forming ferroso-ferric oxide. For details, see U.S.P., p. 164.

For *tests for identity*, for *impurities* (arsenic, sulfide) and for *assay*, see U.S.P., p. 165.

Remarks.—Reduced iron represents a chemically pure form of iron and is supposedly entirely free from carbon. It is prepared by placing subcarbonate of iron (virtually, ferric oxide, Fe_2O_3) in a tube of Pyrex glass or a piece of iron piping, some 4 feet long, and ½ to 1 inch in diameter. Hydrogen, produced in the ordinary way (zinc and acid, see p. 534) is passed through the tube, which is placed in an appropriate coal or gas furnace and heat is applied after the air has been expelled from the tube by the current of hydrogen, which, passing over the heated ferric oxide, reduces it to pure iron by the following reaction:

$$Fe_2O_3 + 3H_2 = Fe_2 + 3H_2O.$$

This explains its synonym, *iron by hydrogen.*

Before removing the reduced iron from the tube, care must be taken to see that the same be perfectly cooled. If the iron be poured out while still hot, its affinity for the oxygen of the air is so great that it directly combines therewith, with the formation of a vivid flame. Such substances which spontaneously ignite when brought into contact with the air are said to be *pyrophoric*, and as a striking illustration may be cited antimony sulfide. Some writers claim that pure reduced iron is not pyrophoric, that phenomenon being caused by presence of ferrous oxide, FeO.

There is at present on the market a quantity of so-called "reduced iron" that is not made by the method described above but is a by-product of other manufacturing processes. Aside from occasionally showing an excess of sulfide, it comes up to all of the chemical requirements of the Pharmacopœia. Its structure however is crystalline rather than amorphous; hence U.S.P. XI prescribes a microscopic test for this chemical.

Reduced iron is a valuable tonic.

Dose.—500 mg. (8 grains).

Iron Therapy.—The use of iron and its compounds as a "chalybeate tonic" dates back to the period of Paracelsus (fifteenth century) and there has been much controversy as to which type of iron—(*a*) the metal itself; (*b*) ferrous salts; (*c*) ferric salts; (*d*) scale salts; (*e*) organic compounds containing iron—is the best remedy for anemia. The discovery of Minot and Murphy (1927–1928) that fresh liver was almost a specific in the treatment of pernicious anemia (see p. 965) has caused renewed interest in iron therapy since pharmacological study of the true action of liver in anemia indicated that this action was largely due to the iron content of liver. Waddell, Hart, Steenbock (1928) showed that iron alone did little for anemia, but iron did cure anemia if small amounts of copper were used along with the iron. As liver contains both copper and iron, its value in anemia seems satisfactorily explained.

Since these facts have been published a number of pharmaceutical specialties containing copper and iron have been put upon the market.

The researches just outlined have led to further pharmacological studies on the relative value of the various medicaments containing iron. It is now generally agreed that the ferrous forms are the best for anemia; that the ferric salts are less effective and that the true organic compounds of iron are the least efficient. Witts (1931) gives the following as the best forms of iron in simple anemia:

Iron and ammonium citrate in 0.8 to 1.6 Gm. doses.

Pills of ferrous carbonate in 0.2 to 0.3 Gm. doses.

Reduced iron in 1.3 to 2.4 Gm. doses.

Clark points out that most of the liquid pharmaceuticals containing iron provide an inadequate dose of the metal.

The following compounds of iron are official:

Ferrous Salts:

Saccharated ferrous carbonate (N.F. VI). At least 15 per cent absolute $FeCO_3$.
Mass of ferrous carbonate. At least 36 per cent absolute $FeCO_3$.
Pills of ferrous carbonate. At least 0.06 Gm. $FeCO_3$ to each pill.
Syrup of ferrous iodide, about 5 per cent absolute FeI_2.
Ferrous sulfate. At least 99.5 per cent absolute $FeSO_4.7H_2O$.
Exsiccated ferrous sulfate (U.S.P. X). At least 80 per cent absolute $FeSO_4$.
Granulated ferrous sulfate (U.S.P. X). At least 99.5 per cent absolute $FeSO_4.7H_2O$.

Ferric Salts:

Ferric chloride (U.S.P. X) contains at least 20 per cent metallic iron.
Solution of ferric chloride contains 10 to 11 per cent metallic iron.
Tincture of ferric chloride contains about 13 per cent absolute $FeCl_3$ or 4.5 per cent metallic iron.
Ferric hydroxide with magnesium oxide. A magma consisting of $Fe(OH)_3$, magnesium sulfate, and water.
Solution of ferric sulfate contains about 10.5 per cent metallic iron.
Solution of iron and ammonium acetate (N.F. VI). A pharmaceutical containing 0.16 to 0.20 Gm. metallic iron to 100 cc.

Scale Salts of Iron:

Iron and ammonium citrate contains at least 16 per cent metallic iron.
Green iron and ammonium citrate contains 14.5 to 16 per cent of metallic iron.
Soluble ferric phosphate (N.F. VI) contains at least 12 per cent metallic iron.

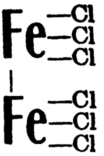
It will be seen that iron compounds in the above table are grouped into ferrous salts, ferric salts, and scale salts of iron. The latter, which are pharmaceutic preparations rather than definite chemicals, will be discussed by themselves (p. 574). The ferrous salts and ferric salts are combinations of acids with iron, the latter exhibiting two different valences.

Reference to the elemental table on p. 390 shows that iron is one of the positive elements which possess more than one valence, and that, while the variation in the valence of negative elements is almost invariably a difference of two—say I, III, V, VII, or II, IV, VI—the variation of iron, expressed in that table, is II and III, the two phases of the element being expressed as ferrous and ferric respectively.

The formulas of ferrous compounds, such as ferrous iodide, FeI_2, or ferrous sulfate, $FeSO_4$, are easy to comprehend if one bears in mind that bivalent iron—iron with two free bonds—act exactly as does bivalent calcium, and all that was said of the formulas of alkaline earth metals on p. 512 applies to ferrous salts.

In giving the valence III to the ferric form clearness is possibly sacrificed for brevity, and it is well to explain that formerly there was discussion on the valence of ferric iron, some giving the valence III (Fe^{III}) and others giving 2 molecules of iron with the valence VI—$(Fe_2)^{VI}$. The latter view was that accepted by the United States Pharmacopœia of 1890, but at the revision of 1900 the trivalent view was accepted, and as a result the formula of ferric chloride is given as $FeCl_3$ in the present Pharmacopœia.

The formula Fe_2Cl_6 is accepted by some chemists (Deville and Troust; also Friedel and Crafts) because, in the first place, the molecular weight estimations place it nearer that of the formula Fe_2Cl_6 than that of $FeCl_3$, and then, too, if the formula Fe_2Cl_6 prevails, it would show the valence of ferric iron to be IV, thus maintaining the regularity in valence variation noticeable in the negative elements. If iron has the valence IV, 2 atoms would link together just as 2 carbon atoms link in ethane (see p. 631), giving the following formula:



Fe_2Cl_6

FERROUS SALTS

Ferrous carbonate, $FeCO_3$, is official in three forms: the saccharated, the mass, and the pills. In all these preparations the carbonate is manufactured in about the same way—treatment of ferrous sulfate with an alkaline carbonate. In the saccharated, sodium bicarbonate is used; and in the other two, potassium carbonate is employed, the reaction in the latter case being—if we use crystallized ferrous sulfate—

$$\begin{array}{ccccccccc} FeSO_4.7H_2O & + & K_2CO_3 & = & K_2SO_4 & + & FeCO_3 & + & 7H_2O. \\ 278 & & 138 & & 174 & & 116 & & 126 \end{array}$$

This means that every 278 Gm. of crystallized ferrous sulfate will produce 116 Gm. of ferrous carbonate. If sodium carbonate is used the reaction will be similar except that sodium sulfate will be the by-product.

Uncombined ferrous carbonate is very unstable, going over into ferric oxide by the following reaction:

$$2FeCO_3 + \underset{\left(\substack{\text{From the}\\ \text{air}}\right)}{O} = 2CO_2 + Fe_2O_3.$$

The iron carbonate or subcarbonate of iron usually found in stores, a red-brown powder, is almost entirely Fe_2O_3—common iron rust. The oxidation of the carbonate may be partly prevented by protecting the salt with sugar, and accordingly we find that all three official preparations just mentioned have sugar as an ingredient.

Ferri Carbonas Saccharatus (U.S.P. X; N.F. VI), or *Saccharated Ferrous Carbonate,* contains in each 100 Gm. not less than 15 Gm. of $FeCO_3$. This pharmaceutical is made by pouring a solution of ferrous sulfate into a solution of sodium bicarbonate, and washing the precipitated ferrous carbonate with boiling water, all the time using precautions to prevent access of air. The washed precipitate is then mixed with sugar, and evaporated to dryness on a water bath, and finally mixed with a sufficient quantity of sugar to make the finished product contain about 15 per cent of ferrous carbonate.

The saccharated carbonate has all the properties of ferrous carbonate, and is a chalybeate tonic, particularly indicated in anemia.

Dose.—250 mg. (4 grains).

MASSA FERRI CARBONATIS—Mass of Ferrous Carbonate

(Mass. Ferr. Carb.—Vallet's Mass)

Mass of Ferrous Carbonate contains not less than 36 per cent and not more than 41 per cent of $FeCO_3$. For assay, see U.S.P., p. 228.

The recipe for this body, commonly called *Vallet's mass,* as well as full details of manufacture, will be found below.

It is made by pouring a solution of ferrous sulfate into a solution of sodium carbonate, removing the resulting sodium sulfate by washing with warm water, to which a sufficient amount of syrup has been added to prevent oxidation; the drained product is then combined with honey and sucrose (sugar). This preparation should contain at least 36 per cent of ferrous carbonate, as is figured out below.

Dose.—250 mg. (4 grains).

LABORATORY EXERCISE

MAKE MASS OF FERROUS CARBONATE

Recipe.—Ferrous sulfate, in clear crystals	20.0 Gm.
Monohydrated sodium carbonate	9.2 Gm.
Honey	7.6 Gm.
Sucrose (sugar), in coarse powder	5.0 Gm.
Syrup, Distilled water, each, a sufficient quantity,	————
To make	20.0 Gm.

Dissolve the ferrous sulfate and the monohydrated sodium carbonate, each separately, in 40 cc. of boiling distilled water, and, having added 4 cc. of syrup to the solution of the iron salt, filter both solutions, and allow them to become cold. Introduce the solution of monohydrated sodium carbonate into a bottle having a capacity of about 100 cc., and gradually add the solution of the iron salt, rotating the bottle constantly or frequently, until carbonic acid gas no longer escapes. Add a sufficient quantity of distilled water to fill the bottle, then cork it and set it aside, so that the ferrous carbonate may subside. Pour off the supernatant liquid, and, having mixed syrup and distilled water in the proportion of 1 volume of syrup to 19 volumes of distilled water, wash the precipitate with the mixture by decantation until the washings no longer have a saline taste. Drain the precipitate on a muslin strainer, and express as much of the water as possible. Lastly, mix the precipitate at once with the honey and sucrose (sugar), and, by means of a water bath, evaporate the mixture in a tared dish, with constant stirring, until it is reduced to 20 Gm.

Chemical Explanation.—When solutions of ferrous sulfate and sodium carbonate are mixed, ferrous carbonate precipitates in the form of a slate-gray solid, viz.:

Ferrous sulfate	plus	Sodium carbonate	give	Ferrous carbonate	plus	Sodium sulfate.
$FeSO_4.7H_2O$	+	$Na_2CO_3.H_2O$	=		+	

Complete this equation.

Ferrous carbonate is a very unstable substance, being converted by action of the atmosphere into red-brown subcarbonate of iron—a mixture of ferrous carbonate and ferric oxide. This change will be noted during the manufacture of the mass in all portions not protected from atmospheric action.

The presence of saccharine matter retards this change, and this explains why the precipitate is washed with water containing syrup, and why the finished product is preserved with sugar and honey. The precipitation is directed to be performed in a flask which is to be kept closed as much as possible, in order to lessen atmospheric action. It will be seen above that the other product of the reaction is sodium sulfate, and the precipitate is to be washed free from this with water and syrup.

Calculations.—The Pharmacopœia directs that the mass contains at least 36 per cent of ferrous carbonate and how near this is to the theoretical amount, the following calculations will show.

Estimate molecular weight of crystalline ferrous sulfate ($FeSO_4.7H_2O$), of monohydrated sodium carbonate ($Na_2CO_3.H_2O$), and of ferrous carbonate, and from the figures work out the following problems:

1. How many grams of monohydrated sodium carbonate will combine with 278 Gm. crystalline ferrous sulfate?
2. How many grams of ferrous carbonate can be made from 278 Gm. of crystalline ferrous sulfate?
3. How many grams of monohydrated sodium carbonate will combine with 20 Gm. of crystalline ferrous sulfate?
4. How many grams of ferrous carbonate can be made from 20 Gm. of crystalline ferrous sulfate?
5. How many grams of ferrous carbonate should there be in 20 Gm. mass of ferrous carbonate?
6. Then what percentage of ferrous carbonate should there be in mass of ferrous carbonate?

Remarks on Process.—The recipe just given is similar to but not identical with that given in the present edition of the Pharmacopœia. The two recipes should be carefully compared by the student.

Dissolve the ferrous sulfate in water in one beaker.

Dissolve the sodium carbonate in water in the other beaker.

Filter the sodium carbonate solution into Erlenmeyer flask, to which a cork should have been previously fitted.

Filter the ferrous sulfate solution into the beaker just emptied after it has been washed and dried.

Cork the Erlenmeyer flask as soon as convenient, after adding the ferrous sulfate solution, but be careful not to allow enough carbon dioxide to collect to explode the flask. Open flask from time to time to let collected gas escape, but only for a moment each time. Be sure to fill flask with water.

Wash precipitate on same kind of strainer used for ferric hydroxide in making ferric citrate (p. 574).

Evaporate mixture in tared dish, that is, in an evaporating dish, the weight of which should first be ascertained.

PILULÆ FERRI CARBONATIS—Pills of Ferrous Carbonate

(Pil. Ferr. Carb.—Chalybeate Pills—Blaud's Pills—Ferruginous Pills)

Each pill contains not less than 0.06 Gm. of $FeCO_3$.

Storage.—Preserve in well-closed containers.

Condensed Recipe.

Rub 8 Gm. potassium carbonate in a mortar with about 5 drops of glycerin; add 16 Gm. of crystalline ferrous sulfate and 4 Gm. of sucrose (sugar) and triturate until a green paste results. Then add 1 Gm. tragacanth and 1 Gm. althea and work into a mass, using more water if necessary. Divide the mass into 100 pills. For details, see U.S.P., p. 291.

It will be seen that these pills, which are commonly called *Blaud's pills,* are made by treating potassium carbonate with ferrous sulfate and sucrose (sugar), glycerin, and water, and finally incorporating althæa and tragacanth as excipients. The mass is cut and rolled into pills. In making these pills it would be well if no reaction took place between the potassium carbonate and ferrous sulfate until the pill had dissolved in the juices of the stomach.

By directing that the mass be beaten thoroughly until it assumes a greenish color, the Pharmacopœia defeats this purpose and affords a product distinctly inferior to Vallet's mass. From the latter the alkaline sulfate has been removed, and the ferrous carbonate is protected by the use of sucrose (sugar) and honey; whereas, the pills, of which we are speaking, still contain the potassium sulfate and a lesser amount of protecting sugar. Leubner claims, however, that the pills, when properly made, keep in good condition as long as fifteen years. Efforts to make Blaud's pills in which the reaction has not taken place has resulted in many ingenious devices: for instance—one firm furnishes a gelatin-coated pill in which the ferrous sulfate is placed in one half and the potassium carbonate in the other half, being separated by a gelatin membrane. The retail pharmacist can easily prepare a similar form of pill, if he so desires, by placing the constituents, one on top of the other, in a gelatin capsule, the two chemicals being separated by a layer of lactose (sugar of milk).

Dose.—3 pills.

Mistura Ferri Composita (U.S.P. VIII; N.F. IV), or *Griffith's mixture,* is made by placing a mixture of myrrh, sucrose (sugar), potassium carbonate, and rose water into a dispensing bottle, adding thereto spirit of lavender, and lastly a solution of ferrous sulfate in rose water.

This preparation should be freshly prepared in the bottle in which it is to be sent out. When the ferrous sulfate is added to the potassium carbonate, an evolution of carbon dioxide usually occurs, and care must be taken to permit the complete escape of this gas before the bottle be corked, otherwise there is danger of the fracture of the flask. The preparation, when fresh, is a bluish-green mixture, but on standing, especially when a few doses have been taken from the bottle, it changes to a brick-dust red—into the so-called "subcarbonate of iron." The instability of this preparation makes its use, at its best, somewhat questionable, and in dispensing it the pharmacist should mention to the purchaser the color change which is bound to occur.

It is used as a ferruginous tonic in tablespoonful doses.

"Fluid" Ferrous Carbonate.—Wilbert has suggested dissolving 3.2 Gm. of granulated ferrous sulfate in 1.5 cc. of water and adding 50 cc. of glycerin; 1.6 Gm. of potassium carbonate are then dissolved in 50 cc. glycerin. These two fluids may be mixed without any precipitation, but on adding any of the mixed fluid to water, the reaction between the sulfate and the carbonate begins with the precipitation of ferrous carbonate. Each 5 cc. of the fluid represents the amount of ferrous carbonate in one Blaud's pill.

Ferrous Chloride, $FeCl_2$, is the leading constituent of *liquor ferri protochloridi* N.F. IV. This is made by preparing a solution of ferrous chloride from card-teeth and a diluted hydrochloric acid and mixing this solution with glycerin and diluted hypophosphorous acid.

Ferrous iodide, FeI_2, is another of the unstable salts of iron, to preserve which it is necessary to add sugar or some other substance capable of preventing oxidation by the atmosphere.

The reaction of manufacture is very simple: $Fe + I_2 = FeI_2$.

As is the case with ferrous carbonate, ferrous iodide is very unstable, splitting, when coming in contact with air, into ferric hydroxide, iodine, and hydriodic acid, as shown in the following equation:

$$FeI_2 + 2H_2O + \underset{\left(\substack{\text{From the}\\ \text{air}}\right)}{O} = Fe(OH)_3 + I + HI.$$

This decomposition is largely obviated by combining ferrous iodide with sugar or hypophosphorous acid.

While former Pharmacopœias recognized three forms of ferrous iodide, U.S.P. XI gives official sanction to only one; the *syrup.*

SYRUPUS FERRI IODIDI—Syrup of Ferrous Iodide

(Syr. Ferr. Iod.—Sirupus ferrosi iodidi concentratus P.I.)

Syrup of Ferrous Iodide contains, in each 100 cc., not less than 6.5 Gm. and not more than 7.5 Gm. of FeI_2, representing approximately 5 per cent of FeI_2, by weight.

Storage.—Preserve in tightly-stoppered bottles.

Summarized Description.

Transparent, pale-yellow, syrupy liquid; sweet, ferruginous taste; slightly acid reaction; sp. gr., 1.37. For details, see U.S.P., p. 375.

For *tests for identity,* for *impurities* (iodine) and for *assay,* see U.S.P., p. 375.

Remarks.—This syrup is made by treating iron with iodine, filtering the solution of ferrous iodide (to which a small amount of sucrose (sugar) has been added) into the rest of the sucrose (sugar), which is dissolved therein with heat. The finished syrup is preserved by addition of a small amount of hypophosphorous acid. The syrup of the present Pharmacopœia contains about 5 per cent by weight of ferrous iodide; that being the approximate strength directed by the new rubric; 6.5 to 7.5 Gm. to 100 cc.

The color of spoiled ferrous iodide can be changed from the brown to the bright green by the addition of a small quantity of card-teeth or reduced iron, this seeming to show that the brown coloration is due to the presence of free iodine, rather than caramel, as has been suggested by one writer. While the problem is still undecided, it behooves the careful pharmacist never to dispense a syrup that has turned brown.

The syrup of ferrous iodide is given as an alterative and chalybeate tonic, diluted with water, and always taken through a tube, as the ferrous iodide attacks the teeth.

Dose.—1 cc. (15 minims).

The author's studies indicate the following facts concerning this syrup:

(*a*) Invert sugar should be used in its manufacture rather than sucrose.

(*b*) Invert sugar is an excellent preservative (stabilizer) for the preparation, whereas hypophosphorous acid is unsatisfactory for the purpose.

(*c*) The syrup (without hypophosphorous acid) keeps excellently when exposed to sunlight. When the acid is present the syrup darkens because of caramelization of the sucrose.

(*d*) The action of sunlight upon the syrup (without hypophosphorous acid) is the complete inversion of the sucrose to dextrose and levulose. It is the levulose that acts as the reducing catalyst.

LABORATORY EXERCISE

MAKE SYRUP OF FERROUS IODIDE

Recipe.—

Iron, in the form of fine, bright wire, and cut into small pieces	2.0 Gm.
Iodine	6.0 Gm.
Hypophosphorous acid	0.5 cc.
Sucrose (sugar)	85.0 Gm.
Distilled water, a sufficient quantity,	
To make	100.0 cc.

Introduce the iron into a flask of thin glass, having a capacity of about 50 cc., add to it 20 cc. of distilled water, and afterward the iodine. Shake the mixture occasionally, checking the reaction, if necessary, by the affusion of cold water, and, when the solution has acquired a greenish color and has lost the odor of iodine, heat it to boiling and add at once 5 Gm. of the sugar; when this has dissolved, filter the solution into the remainder of the sugar contained in a porcelain dish. Rinse the flask and iron wire with 12.5 cc. of distilled water and pass the washings through the filter into the sugar. Stir the mixture with a porcelain or wooden spatula, heating the liquid on a water bath until complete solution is effected, and, having passed the syrup through a clean muslin strainer into a tared bottle, add the hypophosphorous acid and sufficient distilled water to make the product measure 100 cc.

Chemical Explanation.—Ferrous iodide is made by the direct combination of the two elements, iron and iodine, viz.:

Iron plus Iodine equal Ferrous iodide.

$$\mathrm{Fe} + \mathrm{I} =$$

Complete this equation.

Calculations.—Figure out the atomic and molecular weights involved in the above equation, and then solve the following problems:

1. How many grams of iron are needed to make 310 Gm. of ferrous iodide?
2. How many grams of iron are needed to make 7 Gm. of ferrous iodide?
3. How many grams of iodine are needed to make 310 Gm. of ferrous iodide?
4. How many grams of iodine are needed to make 7 Gm. of ferrous iodide?
5. How many grams of ferrous iodide in 100 cc. syrup of syrup ferrous iodide (7 Gm. per 100 cc.)?
6. Then how many grams of iron and iodine are needed to make 100 cc. of syrup of ferrous iodide?
7. Compare these figures with amounts given in official recipe. The slight excess of iron is used to insure complete combination of the iodine.

Remarks on Process.—The recipe just given is similar to but not identical with that given in the present edition of the Pharmacopœia. The two recipes should be carefully compared by the student.

The iron used had best be that form known in commerce as "card-teeth."

Place iron either in Erlenmeyer flask or in large test tube.

After adding the iodine it is well to plug flask with a pledget of cotton to prevent loss of iodine by volatilization.

If reaction is slow on starting, very gentle heat may be employed. *Very gentle* is meant, as anything more will cause loss by volatilization.

If reaction becomes violent, check it by holding flask under running water.

Keep in completely filled bottles, else it turns brown with decomposition of the ferrous iodide. One-ounce bottles well corked are indicated.

Ferri Iodidum Saccharatum (U.S.P. 1890) was made by preparing a solution of ferrous iodide by treatment of iodine with iron wire, mixing the filtered solution with lactose (sugar of milk), evaporating to a dry mass, and then mixing with sufficient lactose (sugar of milk) to make a product containing 20 per cent of ferrous iodide.

This product was very unstable, and hence was wisely omitted from the Pharmacopœia.

Pilulæ Ferri Iodidi (N.F. VI), or *Pills of Ferrous Iodide*, are made by triturating reduced iron, iodine, and water until the red tint has disappeared; mixing with glycyrrhiza, sucrose (sugar) extract of glycyrrhiza and acacia, beating the mass to a pilular consistence, and coating the pills with gelatin.

Each pill contains about 1 grain of ferrous iodide.

Dose.—2 pills.

Ferri Lactas (U.S.P. 1890; N.F. V) or *Ferrous Lactate*, $Fe(C_3H_5O_3)_2 + 3H_2O$, is the ferrous salt of lactic acid (the composition of which will be found described on p. 677) and is made by treating lactic acid with reduced iron, and subsequently evaporating the solution to dryness.

This compound is the iron constituent of the formerly official *syrup of hypophosphites with iron*, where it was used because it was supposed to be a most easily assimilable salt of iron. This claim has never been thoroughly substantiated, and the preparation is one of doubtful value.

The lactate is administered in 5-grain doses.

Ferrous sulfate ($FeSO_4$), called "green vitriol," from the Latin *vitreus*, glass, because the crystals look like green glass. When we distil these crystals, an oily liquid passes over, and this the alchemists of three hundred years since called "oil of vitriol," a name that still clings to the distillate—sulfuric acid.

In an impure form ferrous sulfate is called "copperas," although containing no copper whatever.

Ferrous sulfate was official in U.S.P. X in three forms: the crystalline, containing 7 molecules of water of crystallization; the granulated, which contains the same amount of water as do the crystals (turn to Granulation on p. 174), and, lastly, the exsiccated, which represents the crystalline minus the greater quantity of its water, 100 parts of the crystals yielding 64 parts of the exsiccated. In U.S.P. XI only the crystalline form is official. The dried is preferable to the crystalline in the manufacture of pills, being of lesser bulk and not producing a soft mass. Note in these two forms—the crystalline and the dried—an interesting demonstration of the influence of water of crystallization on a substance. Dried ferrous sulfate is a grayish-white, opaque powder; while the crystals, which differ from the dried only by the presence of water of crystallization, are green and transparent.

FERRI SULFAS—Ferrous Sulfate

(Ferr. Sulf.—Iron Sulfate)

$FeSO_4.7H_2O$. Molecular weight, 278.01

Ferrous Sulfate contains not less than 54.36 and not more than 57.07 per cent of anhydrous ferrous sulfate ($FeSO_4$), corresponding to not less than 99.5 per cent of the hydrated salt ($FeSO_4.7H_2O$).

Storage.—Preserve in air-tight containers.

Summarized Description.

Pale, bluish-green, efflorescent, monoclinic prisms or in granules; saline styptic taste; oxidizes on exposure to air, becoming coated with brown-yellow basic ferric sulfate; soluble in about 1.4 parts of water; insoluble in alcohol. For details, see U.S.P., p. 163.

For *tests for identity*, for *impurities* (free acid, heavy metals) and for *assay*, see U.S.P., p. 163.

Remarks.—This salt is made by treating scrap iron with sulfuric acid, and evaporating the solution to a point where the green crystals will be obtained. These green crystals are not very stable, comparatively readily combining with oxygen of the air, with the formation of basic ferric sulfates by the following reactions:

$$(a)\ 2FeSO_4 + O = Fe_2O(SO_4)_2.$$
$$(b)\ 2FeSO_4 = Fe_2O_2SO_4 + SO_2.$$

The present Pharmacopœia directs that this brown efflorescent salt must not be used for any official purpose.

In order to insure the formation of a perfectly green ferrous sulfate, it is usually advisable to crystallize from acid solution containing some card-teeth, the latter acting on the acid with the constant evolution of hydrogen. Thus, cheap copperas can be converted into beautiful crystals of ferrous sulfate by dissolving in water, adding a small quantity of sulfuric acid and some card-teeth, and warming gently until a green solution is obtained. This is filtered from the undissolved ferric oxide and allowed to crystallize.

Ferrous sulfate is used as an astringent and chalybeate tonic.

Dose.—200 mg. (3 grains).

Ferri Sulfas Granulatus (U.S.P. X), or *Granulated Ferrous Sulfate,* represents ferrous sulfate in the form of small crystals called granules. Its description is now included in the monograph for *Ferri Sulfas,* U.S.P. XI (see above). It is prepared by dissolving ferrous sulfate in water containing diluted sulfuric acid, evaporating to a certain degree of concentration, and stirring the mixture while it is cooling. (See p. 174.) In this way the salt separates into small crystals, which are immediately transferred to a funnel, stoppered with a plug of cotton, the mother liquid allowed rapidly to drain off, and the crystals then freed from the remaining adhering water| by pouring on a small quantity of alcohol; the object of washing with alcohol being to dry the granules as rapidly as possible, and that without a loss of water of crystallization. Full details of manufacture are given on page 174. It should be emphasized that, theoretically, granulated ferrous sulfate contains exactly the same amount of water as does the crystalline, although in practice it usually loses a small amount of its water of hydration by efflorescence.

Dose.—100 mg. (1¼ grains).

Ferri Sulfas Exsiccatus (U.S.P. X), or *Exsiccated Ferrous Sulfate,* represents the equivalent of not less than 80 per cent of anhydrous ferrous sulfate. It is made by efflorescing crystallized ferrous sulfate and then exsiccating on a water bath; 100 Gm. of the crystallized yielding 64 to 65 Gm. exsiccated salt.

It will be seen that the exsiccated salt is a much more concentrated preparation than the crystalline, and, therefore, for a similar dose, about three fifths as much need be given. It is admirably adapted for pills, since the same amount of ferrous sulfate can be given in the exsiccated form in a much smaller bulk.

Dose.—60 mg. (1 grain.)

Ferrous Oxalate (U.S.P. 1890), FeC_2O_4, is made by treating ferrous sulfate with oxalic acid, and this process explains the value of oxalic acid as a remover of ink stains. Most black ink is tannate of iron, and if to this oxalic acid be added, the tannic acid is replaced by oxalic acid, and the resulting ferrous oxalate leaves a light yellow stain, instead of the pronounced black of the ink, and while the stain is as insoluble as is ink, it does not show. In using oxalic acid for this purpose great care must be taken lest it injure the fabric.

FERRIC SALTS

Having already given the structure of ferric salts our careful consideration, we can proceed to the discussion of the compounds themselves, commencing with one that will thoroughly explain the transition from the ferrous to the ferric state, namely:

Ferri Chloridum (U.S.P. X), or *Ferric Chloride,* contains $FeCl_3$ in a hydrated form corresponding to not less than 20 per cent of Fe. In making this salt we first treat iron with hydrochloric acid, which gives us ferrous chloride, $FeCl_2$, by the following reaction:

$$Fe + 2HCl = H_2 + FeCl_2.$$

It is important to note that usually a metal treated with an acid will yield an "ous" salt of that metal; that salt exhibiting the metal in its lowest valence. Hence we get in this case ferrous chloride, which is analogous to ferrous oxide, which we do not want. We wish ferric chloride, and how are we to get it? How did we make sulfuric oxide from sulfur*ous* oxide? By oxidizing with nitric acid; and that is exactly what we do with ferrous chloride to change it into ferric chloride; the reaction being:

$$6FeCl_2 + 6HCl + 2HNO_3 = N_2O_2 + 4H_2O + 3Fe_2Cl_6.$$

Compare this reaction with that of the conversion of sulfurous oxide to sulfuric oxide, given on p. 447, and the analogy will be noted.

The 3 molecules of HNO_3 break into N_2O_2, H_2O and 3 atoms of oxygen, and on the basis of the 3 atoms of oxygen, yielded by the 2 molecules of nitric acid, hangs the entire proportion of the equation.

Note that in this oxidation the oxygen does not combine with the iron, but that it seizes the hydrogen of the hydrochloric acid, setting the chlorine free and giving it a chance to combine with the iron of the ferrous chloride. This is a confirmation of the assertion on p. 447 that the function of an oxidizing agent is not merely that of adding oxygen to a substance, but that its main effort is toward raising the valence of one of the elements entering into the reaction. Moreover, the element whose valence is raised is not necessarily the one which is oxidized.

In practice, ferric chloride is first made in the form of the official solution and this is then evaporated to about 40 per cent of its original weight and the residue is set aside until it forms a crystalline mass.

Ferric chloride is used as a styptic externally, and internally as a tonic.

Dose.—60 mg. (1 grain).

LIQUOR FERRI CHLORIDI—Solution of Ferric Chloride

(Liq. Ferr. Chlor.—Solution of Iron Perchloride)

Solution of Ferric Chloride is an aqueous solution containing ferric chloride ($FeCl_3$), corresponding to not less than 10 per cent and not more than 11 per cent of Fe.

It contains not less than 3 per cent and not more than 5 per cent of HCl.

Storage.—Preserve in glass-stoppered bottles, in a cool place and protected from light.

Condensed Recipe (U.S.P. IX).

Heat 125 Gm. card-teeth (p. 556) with a mixture of 420 Gm. hydrochloric acid with 250 cc. of distilled water on a water bath until effervescence ceases (or for one and one-fourth hours). Then boil the mixture, filter, wash the filter with hot distilled water, add to the filtrate 220 Gm. hydrochloric acid, and add the mixture to 65 Gm. nitric acid contained in a large porcelain evaporating dish. Then warm gently, add more nitric acid if the liquid is black and warm until the liquid is clear reddish-brown and until effervescence ceases. Then evaporate in a sand bath until free from nitric acid, adding water as necessary. Lastly, add 40 Gm. hydrochloric acid and enough water to make 1000 Gm.

Summarized Description.

Reddish-brown liquid; acid, strongly styptic taste; acid reaction; sp. gr. 1.29 to 1.32. For details, see U.S.P., p. 209.

For *tests for identity*, for *impurities* (zinc, copper, lead, alkaline salts, nitric acid, ferrous salts) and for *assay*, see U.S.P., p. 209.

This preparation contains about 29 per cent of anhydrous salt, the solution containing an excess of free hydrochloric acid. It is rarely administered in medicine, the tincture of ferric chloride being preferred for internal use, and Monsel's solution is better for external styptic purposes.

Dose.—0.1 cc. (1½ minims).

Liquor Ferri Oxychloridi (N.F. IV) is made by preparing ferric hydroxide from solution of ferric chloride and ammonia water and then adding to the washed magma, hydrochloric acid (not quite enough to make a normal chloride), glycerin and water. According to Krantz, this is really a solution of colloidal ferric hydroxide in molecularly dispersed ferric chloride.

TINCTURA FERRI CHLORIDI—Tincture of Ferric Chloride

(Tr. Ferr. Chlor.—Tincture of Iron)

A hydro-alcoholic solution containing, in each 100 cc., about 13 Gm. of $FeCl_3$, corresponding to not less than 4.5 Gm. of Fe.

Storage.—Preserve in glass-stoppered bottles, in a cool place and protected from light.

Condensed Recipe.

Mix 350 cc. of solution of ferric chloride with enough alcohol to make 1 liter. For details see U.S.P., p. 399.

Summarized Description.

Bright, amber-colored liquid; slightly ethereal color; astringent styptic taste; acid reaction; sp. gr. 1. For details, see U.S.P., p. 399.

For *tests for identity*, for *impurities* (nitric acid; ferrous salt) and for *assay*, see U.S.P., p. 399.

Remarks.—This galenic preparation is made by combining 350 cc of solution of ferric chloride with alcohol, to make 1000 cc. Former Pharmacopœias directed that the mixture should stand for three months before dispensing, in order that the free hydrochloric acid found in the solution will have time to react on the alcohol and form compound ethers, which render it more active. This requirement is omitted from U.S.P. XI.

It is sometimes confusing to a student to read superficially that this tincture contains 35 per cent of the solution, which contains about 29 per cent of ferric chloride and then note that the actual ferric chloride content of the tincture is about 13 per cent. The following figures show, however, that the latter statement is correct:

1000 cc. of tincture of ferric chloride contain 350 cc. of solution of ferric chloride.

1000 cc. of the tincture weigh the same as water, 1000 Gm.

1000 Gm. of the tincture contain 350 cc. of the solution.

1000 Gm. of the solution contain 290 Gm. of dry ferric chloride.

1000 Gm. of the solution measure 1000 ÷ 1.3 or 769 cc.

769 cc. of the solution contain 290 Gm. of dry ferric chloride.

350 cc. of the solution contain $^{350}/_{769} \times 290$ or almost 131.9 Gm. of dry ferric chloride.

Hence 1000 Gm. of the tincture contain 350 cc. of solution or 131.9 Gm. of ferric chloride; hence the tincture contains 13.19 per cent $FeCl_3$.

The tincture of ferric chloride is one of the most satisfactory means for the administration of iron. The chief objection is the fact that, when taken directly into the mouth, it is apt to injure the teeth, due partly to the iron, but chiefly to the excess of acid present in the preparation. It is, therefore, generally directed to be administered largely diluted with water and sucked through a tube. A very simple and effective method of administration, totally devoid of any danger of injuring the teeth, is to drop the dose of the tincture into a gelatin capsule of appropriate size, say, No. 2 or No. 3, and then swallow the same immediately in a draught of water. Such capsules are unstable, the water in the tincture dissolving the gelatin, and hence must be made by the patient at the moment of administration—a very simple matter when the proper directions are given.

Dose.—0.6 cc. (10 minims).

The tincture of ferric chloride is an ingredient of the *solution of iron and ammonium acetate* (N.F. VI). (See p. 572.)

McNair states that a 5 per cent solution of ferric chloride in 50 per cent alcohol is of value in rhus poisoning (p. 877).

Tinctura Ferri Citrochloridi (N.F. VI) was devised by Cruse, under the name of *tasteless tincture of iron* and is made by treating solution of ferric chloride with sodium citrate and adding alcohol and water. It is a beautiful green fluid and is valuable inasmuch as prescriptions calling for tincture of ferric chloride along with alkaline phosphates can frequently be compounded without precipitation, if the equivalent quantity of the tincture of the citrochloride is employed. Like tincture of ferric chloride U.S.P. the tincture of citrochloride represents 350 cc. of the official solution to the liter.

Tinctura Ferri Chloridi Ætherea (N.F. V) or *Bestuscheff's Tincture,* is an ethereal tincture of ferric chloride. It is made by mixing 60 parts of the official solution of ferric chloride with enough of a mixture of alcohol and ether to make 1 liter and letting the mixture stand in the sunlight until it is bleached.

Ferri Hypophosphis (N.F. VI) or *Ferric Hypophosphite* has been supposed to have the formula $Fe(PH_2O_2)_3$. Weinland and Hieber, however, find that hypophosphorous acid forms with trivalent iron complex bodies such as $Fe_3(OH)(PH_2O_2)_8$, $Fe_4(OH)(PH_2O_2)_9$, $Fe_7(PH_2O_2)_{19}(OH)_2$, etc.

This salt is made by treating a solution of calcium hypophosphite with a solution of ferric chloride, when ferric hypophosphite is produced by the following reaction:

$$3Ca(PH_2O_2)_2 + Fe_2Cl_6 = 2Fe(PH_2O_2)_3 + 3CaCl_2.$$

In this case calcium chloride dissolves, while the ferric hypophosphite precipitates, is collected, washed, and dried.

Ferric hypophosphite possesses properties similar to all hypophosphites, with the additional advantage of being a chalybeate tonic. It is given in 3-grain doses.

Liquor Ferri Hypophosphis (N.F. IV) is a 16.5 per cent solution of ferric hypophosphite in glycerin and water; potassium citrate being added to facilitate the dissolving of the iron salt.

Ferric Valerianate (U.S.P. 1890), $Fe(C_5H_9O_2)_3$, is the ferric salt of valerianic acid, the chemistry of which will be found on p. 687. It is made by the double decomposition of sodium valerianate with ferric sulfate, the reaction being as follows:

$$6NaC_5H_9O_2 + Fe_2(SO_4)_3 = 3Na_2SO_4 + 2Fe(C_5H_9O_2)_3.$$

The insoluble ferric valerianate thus produced is separated from the sodium sulfate by filtration and subsequent washing of the precipitate.

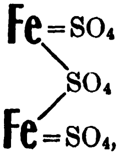
The ferric valerianate is given as a tonic and nervine in doses of from 0.3 to 0.6 Gm. (5–10 grains).

Ferri et Ammonii Sulfas (U.S.P. VIII), or *Ferric Ammonium Sulfate*, is the well-known *ferric alum*, the chemistry of which was explained on p. 547 among the other alums, hence we only need to emphasize the analogy between the official alum and ferric alum:

Alum (U.S.P.) is	$K_2SO_4Al_2(SO_4)_3.24H_2O$.
Ferric alum is	$(NH_4)_2SO_4Fe_2(SO_4)_3.24H_2O$.

Ferric alum is made by combining molecular quantities of the solution of ferric sulfate with a solution of ammonium sulfate. On evaporating the mixture the pure crystals of ferric alum separate, leaving the dark-brown mother liquor. As already mentioned on p. 547, ferric alum possesses very few of the properties of the average iron salt, being much more similar to the alums.

It is used as styptic and very rarely internally.

Ferric sulfate, $Fe_2(SO_4)_3$, which is graphically  is official in the form of a *solution* containing about 36 per cent of ferric sulfate—called liquor ferri *ter*sulfatis, to distinguish it from the formerly official solution of the basic salt, *liquor ferri subsulfatis*, which is commonly called "Monsel's solution."

LIQUOR FERRI TERSULFATIS—Solution of Ferric Sulfate (Liq. Ferr. Tersulf.—Solution of Iron Tersulfate)

An aqueous solution containing ferric sulfate $[Fe_2(SO_4)_3]$, corresponding to not less than 9.5 per cent and not more than 10.5 per cent of Fe.

Summarized Description.

Yellowish-brown liquid; acid, strongly styptic taste; acid reaction; miscible with alcohol and with water; sp. gr. 1.430. For details, see U.S.P., p. 210.

For *tests for identity*, for *impurities* (nitric acid, ferrous salt) and for *assay*, see U.S.P., p. 210.

Remarks.—Solution of ferric sulfate is made by the oxidation of ferrous sulfate with nitric acid, and by a process entirely analogous to that described under the head of ferric chloride. For details see below.

As in the care of ferric chloride, it is seen that, to accomplish this result, not only is nitric acid necessary, but also an additional quantity of the characteristic acid, in this case sulfuric acid, the amount of the latter being directly proportional to the difference in SO_4 groups expressed in the two formulas, ferrous sulfate and ferric sulfate.

The solution of tersulfate of iron is one of the most important of the iron preparations, although very rarely called for in prescriptions or at the counter. It is the basis of all the scale salts of iron, and is the iron constituent used in preparing the antidote for arsenic. For this reason, if for no other, the pharmacist must keep in stock a solution of tersulfate of iron.

It is worth noting that the ferric sulfate of this preparation is the true persulfate of iron, though, through an unfortunate blunder, custom has established the precedent of calling the solution of subsulfate of iron "solution of persulfate of iron."

LABORATORY EXERCISE

MAKE SOLUTION OF TERSULFATE OF IRON

Recipe.—	Ferrous sulfate in clear crystals	62.5 Gm.
	Sulfuric acid	12.0 Gm.
	Nitric acid,	
	Distilled water, each, a sufficient quantity,	————
	To make	125.0 Gm.

Add the sulfuric acid to about 30 cc. of distilled water in a capacious porcelain dish, heat the mixture to nearly 100° C., then add 7 Gm. of nitric acid, and mix well. Divide the ferrous sulfate, coarsely powdered, into four equal portions, and add these portions, one at a time, to the hot liquid, stirring after each addition until effervescence ceases. When all the ferrous sulfate is dissolved, if the solution has acquired a black color, add nitric acid, a few drops at a time, heating and stirring until it no longer causes red fumes to be evolved, and the solution assumes a clear, reddish-brown color; then boil the liquid until it is free from nitric acid. Lastly, add enough distilled water to make the product weigh 125 Gm. Filter if necessary.

Chemical Explanation.—This solution is prepared by the oxidation of green ferrous sulfate, $FeSO_4$, to red-brown ferric sulfate, $Fe_2(SO_4)_3$, through oxidizing action of nitric acid in the presence of sulfuric acid. The need of this extra sulfuric acid is shown in comparison of the formulas of ferrous sulfate and ferric sulfate respectively:

Ferrous sulfate	*Ferric sulfate*
$FeSO_4$	$Fe_2(SO_4)_3$

$2FeSO_4$ or $Fe_2(SO_4)_2$ in changing to $Fe_2(SO_4)_3$,

requiring an extra SO_4 group.

The oxidizing action of nitric acid is fully explained on p. 447 and there it is shown that every 2 molecules of nitric acid give 3 atoms of oxygen in oxidations. With these hints construct the equation representing the reaction, viz.:

Ferrous sulfate plus sulfuric acid plus nitric acid equals ferric sulfate plus nitrogen dioxide plus water.

Note that the red fumes given off during the reaction are not N_2O_2, but are N_2O_4, which is formed the moment the colorless gas N_2O_2, comes in contact with air, viz.:

$$N_2O_2 + O_2 = N_2O_4.$$

Calculations.—Figure out molecular weight of crystallized ferrous sulfate ($FeSO_4 \cdot 7H_2O$), sulfuric acid, nitric acid, and ferric sulfate, and with these figures work out the following problems:

1. How many grams of crystalline ferrous sulfate, 100 per cent sulfuric acid, and 100 per cent nitric acid needed to make 1200 Gm. of ferric sulfate?

2. How many grams of 94 per cent sulfuric acid needed to make 1200 Gm. of ferric sulfate?

3. How many grams of 68 per cent nitric acid needed to make 1200 Gm. of ferric sulfate?

4. How many grams of ferric sulfate are contained in 125 Gm. of solution of ferric sulfate, U.S.P., which is 36 per cent $Fe_2(SO_4)_3$?

5. How many grams of crystalline ferrous sulfate, 94 per cent sulfuric acid, and 68 per cent nitric acid needed to make 45 Gm. ferric sulfate?

6. Then how many grams of these three constituents needed to make 125 Gm. of solution of ferric sulfate, U.S.P.?

Remarks on Process.—The recipe just given is similar to but not identical with that given in U.S.P. X. The two recipes should be carefully compared by the student.

Mix sulfuric acid and water in tared pint evaporating dish, carefully pouring acid into water and not the reverse.

Add the ferrous sulfate gradually, letting reaction end before adding another of the four portions.

Add the nitric acid fairly generously. If you get an excess, it can be driven off by heating mixture. Do not add too much, however, as it will be wasteful of the acid, and will also require long heating to drive it all off.

If the liquid is black, it means an insufficiency of nitric acid. Add some, and the red tint will come, accompanied by evolution of N_2O_4 fumes.

Boil until free from nitrous odor, that is, the choking odor of nitric acid and of N_2O_4. Experience will readily teach you the odor.

Add water to make product weigh 125 Gm. To do this easily, be sure to tare the dish before starting.

Liquor Ferri Subsulfatis (N.F. VI) is commonly called Monsel's solution. The prefix "sub" means a basic salt—a combination of an oxide of a metal with a salt of the same metal. Thus, ferric *sub*sulfate is a combination of ferric sulfate and ferric oxide; bismuth *sub*nitrate is a combination of bismuth nitrate and bismuth oxide; and so on. Note that in the definition given in N.F. VI, no symbolic formula is assigned the iron salt found in Monsel's solution. In the Pharmacopœia of 1880 the formula was given as $Fe_4O(SO_4)_5$, which may be untangled as follows:

If we take 3 molecules $Fe_4O(SO_4)_5$ we get .... $F_{12}O_3(SO_4)_{15}$
Subtract from this .... Fe_2O_3

We have left .... $Fe_{10}(SO_4)_{15}$.
Or .... $5Fe_2(SO_4)_3$.

In other words, 5 molecules of ferric sulfate and 1 molecule of ferric oxide give 3 molecules of ferric subsulfate.

Both solutions—of ferric subsulfate and of ferric tersulfate—are made from ferrous sulfate—just as ferric chloride was made from ferrous chloride—by oxidation with nitric acid, the reaction in making ferric tersulfate being:

$$6FeSO_4 + 3H_2SO_4 + 2HNO_3 = 3Fe_2(SO_4)_3 + N_2O_2 + 4H_2O.$$

Compare this to the equation in making subsulfate, viz.:

$$12FeSO_4 + 3H_2SO_4 + 4HNO_3 = 3Fe_4O(SO_4)_5 + 2N_2O_2 + 5H_2O.$$

This shows that while 3 molecules of sulfuric acid are used in both reactions, that quantity suffices for 6 molecules of ferrous sulfate in making the tersulfate, and for 12 molecules of ferrous sulfate when the subsulfate is made. In other words, in making the tersulfate from a given quantity of ferrous sulfate, twice as much sulfuric acid is required as is needed to make the subsulfate. The N_2O_2 of the equations just given is a colorless gas, which on coming in contact with the air is instantly converted into N_2O_4, which we met in the sulfuric acid manufacture and which form the red fumes spoken of in the recipe for the tersulfate solution, as given above.

Note that Monsel's solution—the *sub*sulfate—is to be dispensed when the *per*sulfate is called for.

As just mentioned above, the solution of subsulfate of iron differs from the solution of tersulfate of iron in that it is made from less sulfuric acid and more ferrous sulfate. This is best shown by a comparison of the quantities of the ingredients of the two solutions as given in U.S.P. IX:

	Ferrous Sulfate	Sulfuric Acid	
Solution of tersulfate	500 Gm.	96 Gm.	to 1000 Gm. finished product.
Solution of subsulfate	675 Gm.	65 Gm.	

N.F. VI directs the use in making solution of subsulfate of iron of 1045 Gm. ferrous sulfate and 55 cc. sulfuric acid to 1000 cc.; volume-weight quantities that are approximately the same as the weight-weight quantities just cited.

One of the simplest tests of distinction between the two solutions is the behavior of each when treated with an equal quantity of concentrated sulfuric acid. Under such treatment the subsulfate forms a semisolid mass, while the tersulfate forms a clear, limpid liquid.

The solution of subsulfate of iron is a favorite styptic and astringent, used for staunching the flow of blood, and is rarely given internally. The residue from the evaporation of the solution, termed *Monsel's powder* in commercial usage, is very largely used for this purpose, especially in barber shops for the drying up of cuts produced in shaving.

Dose.—0.2 cc. (3 minims).

Magma Ferri Hydroxidi (N.F. IV), or *Ferri Hydroxidum* (U.S.P. VIII), is ferric hydroxide $Fe(OH)_3$ and is produced by pouring a diluted solution of ferric sulfate into a diluted ammonia water; the equation showing the reaction being

$$Fe_2(SO_4)_3 + 6NH_4OH = 2Fe(OH)_3 + 3(NH_4)_2SO_4.$$

It is a red-brown, thick tenacious precipitate, called a "magma," already mentioned (p. 167).

In making this preparation, it is very important that the tersulfate solution be added to the diluted ammonia. If the reverse operation is performed, we obtain an oxyhydrate rather than the hydroxide itself.

Since ferric hydroxide very rapidly decomposes into water and ferric oxide, which is insoluble even in acids, it must be freshly prepared when wanted, and since when needed for poisoning with arsenic, it must be dispensed with the least possible loss of time, every pharmacist should keep on hand diluted solutions of ammonia water and of ferric sulfate. Moreover, in order to expedite matters, it is advisable to place convenient to the bottles holding these two solutions strainers and their required paraphernalia. Since the dispensing of these preparations for poisoning by arsenic, fortunately, does not occur every day, this outfit may rest on the shelf for years without being used. Such being the case, it is advisable to renew, from time to time, the diluted ammonia water. The diluted solution of ferric sulfate keeps perfectly. When dispensed as an antidote for arsenic poisoning, haste is the prime requirement, and hence the pharmacist need not bother about washing the precipitate completely free from the ammonium sulfate. All that is necessary is to free the magma from ammonia water. In practice it is best to prepare rapidly a small quantity of the magma, say, 1 or 2 ounces, in a very incomplete way, and despatch this to the sufferer with the promise of an additional quantity to be sent later on. However, for the purpose of an antidote for arsenic *ferric hydroxide with magnesia* (p. 572) is preferred.

For chemical purposes, such as for the manufacture of scale salts and the detannating of pharmaceuticals, the ferric hydroxide so employed should be totally free from ammonium sulfate. The process of washing the precipitate is very tedious. The writer, for such purposes, has poured the magma on large canvas strainers of texture sufficiently coarse to permit the passage of water. Through such strainers, however, a considerable quantity of the magma is apt to escape at first, and in order that none of this be lost, the strainers are arranged in a rack, so that tiers of at least three such strainers are employed. In this way the magma passing through the top strainer had a chance to collect on the second strainer, and that which passed through the second strainer was almost sure to be retained by the third one. Beneath the third strainer a suitable receptacle for collecting the drippings was placed. After the precipitate, with its supernatant liquor, had been transferred to the strainers, the wash water was introduced into the top strainer by means of a siphon, so regulated that the amount of water dripping through exactly replaces the amount of water dripping therefrom. In this way large quantities of magma can be readily washed within twelve to eighteen hours.

Ferric hydroxide was introduced into medicine by reason of its value as an antidote for arsenic, the discovery of this property being made by Bunsen and Berthold in 1834, its efficiency being due to the formation of the insoluble ferric arsenic, as shown in the following equation:

$$3As_2O_3 + 2Fe(OH)_3 = 2Fe(AsO_2)_3 + 3H_2O.$$

There is now some difference of opinion as to its value as arsenic antidote.

For antidotal purposes it is administered in tablespoonful doses, followed by an emetic, and, as mentioned above, the ferric hydroxide with magnesia is now considered preferable.

Pharmaceutically, ferric hydroxide is the basis of the scale preparations of iron.

Dialyzed iron is an unofficial modification of ferric hydroxide, and has already been discussed as a type of the products of dialysis (p. 177).

This preparation was originally made by treating solution of ferric chloride with freshly precipitated ferric hydroxide. It is now usually made by treating solution of ferric chloride with ammonia water. The mixture is placed on the dialyzing membrane, when crystalline substances, ammonium chloride and ferric chloride, pass through the septum, leaving colloidal ferric oxychloride, of composition varying from

Fe_2Cl_6, $11Fe_2O_3$ to Fe_2Cl_6, $31Fe_2O_3$. Physical chemists, however, consider it a colloidal solution of ferric hydroxide; Smith and Giesy finding no indication of the presence of oxychloride.

Dialyzed iron is a limpid, red-brown liquid, free from acidity and without styptic taste. It is used as a tonic in doses of 5 to 30 drops.

MAGMA FERRI HYDROXIDI—Magma of Ferric Hydroxide

(**Magma Ferr. Hydrox.**—Arsenic Antidote, Ferri Hydroxidum cum Magnesii Oxido U.S.P. X)

Condensed Recipe.

Mix 40 cc. of solution of ferric sulfate with 125 cc. of water; and keep it in an appropriate bottle. Triturate 10 Gm. magnesium oxide with enough water to make a thin paste and keep it in a liter bottle, adding enough water to make paste measure about 750 cc. On call, add the ferric solution to the well-shaken paste and then dispense. The magnesium oxide may be replaced by 300 cc. of Magnesia Magma, U.S.P. For details, see U.S.P., p. 222.

It will be seen that this preparation is made by treating diluted solution of ferric sulfate with the milk of magnesia (that is, magnesia rubbed with water), the reaction being:

$$2Fe_2(SO_4)_3 + 6Mg(OH)_2 = 4Fe(OH)_3 + 6MgSO_4.$$

The result of this reaction, as will be noticed, is practically the same as in the method of making pure ferric hydroxide. The great advantage, however, is that the magma thus produced is efficient without washing, because the impurities are the mild alkali, magnesium hydroxide, and the harmless magnesium sulfate. These two compounds also serve antidotal purposes by reason of the formation of the insoluble magnesium arsenite. For this reason this preparation is greatly to be preferred over the pure ferric hydroxide as an antidote for arsenic, it being rapidly prepared by the blending of the diluted solution of ferric sulfate with a magnesia mixture, followed by the rapid removal of the superfluous water by straining. The Pharmacopœia directs that the diluted solutions of ferric sulfate and the milk of magnesia should be kept on hand by the pharmacist, for instant admixture in cases of arsenical poisoning.

Dose.—Arsenical antidote, 120 cc. (4 fluidounces).

Ferri Oxidum Saccharatum (N.F. VI) is made by preparing ferric hydroxide from solution of ferric chloride and sodium carbonate, mixing the washed magma with sucrose (sugar), dissolving the mixture in a 15 per cent solution of sodium hydroxide and then evaporating the solution to dryness on a water bath. It contains about 3 per cent of iron.

Liquor Ferri et Ammonii Acetatis (N.F. VI), or *Solution of Iron and Ammonium Acetate,* is made by mixing together 500 cc. of a slightly acid solution of ammonium acetate, 60 cc. of diluted acetic acid, 40 cc. of tincture of ferric chloride; 120 cc. of aromatic elixir, 120 cc. of glycerin and enough distilled water to make 1 liter. It is a clear, reddish-brown liquid; with sweetish saline then slightly astringent taste; aromatic odor; sp. gr. 1.039.

In mixing the chemicals as above described, ferric acetate is produced, and a brilliant garnet solution ensues. In preparing the solution, it is important that the full amount of acetic acid be employed, for if the solution is not distinctly acid, the basic acetate of iron will separate as an unsightly red-brown precipitate.

The same precipitate occurs in a properly prepared solution, when it becomes old, hence the Formulary direction as to preparing freshly.

Basham's mixture, as this solution is called, is a popular tonic in some sections.

Dose.—15 cc. (4 fluidrachms).

Solution of Ferric Acetate (U.S.P. 1890; N.F. IV).—This preparation, containing 31 per cent of the anhydrous salt, is made by dissolving freshly prepared ferric hydroxide in the molecular quantity of glacial acetic acid.

The solution of ferric acetate is used as a mild chalybeate tonic, and in doses of 2 to 10 minims.

Solution of Ferric Nitrate (U.S.P. 1890; N.F. IV).—This preparation, containing 1.3 per cent metallic iron, is made by a process very similar to that used in making the solution of ferric acetate; the ferric hydroxide in this case being dissolved in the molecular quantity of nitric acid. This solution is interesting by reason of the light tint which it possesses; most of the other ferric solutions are of a brilliant garnet red, but this one usually possesses a color scarcely darker than amber.

Solution of Ferric Citrate (U.S.P. 1890; N.F. V).—Recipe and details of manufacture, see below.

This solution, like the two just discussed, is made by treating ferric hydroxide with an appropriate acid; in this case, citric acid. If to the drained magma, crystals of citric acid are added, and the mixture placed on a water bath for a few minutes, the magma is converted into a clear garnet red solution, usually weaker than the strength prescribed in N.F. V. It is, therefore, evaporated on a water bath at a temperature not exceeding 60° C. This shows that a large amount of water is mechanically held by the ferric hydroxide, its absorbing capacity being almost as great as that of aluminum hydroxide.

The solution of ferric citrate affords a convenient liquid form of that valuable remedy—ferric citrate. It contains about 50 per cent of ferric citrate, and will be found of great convenience in the dispensing of prescriptions directing ferric citrate dissolved in water, since the dissolving of ferric citrate is quite tedious.

LABORATORY EXERCISES

MAKE SOLUTION OF FERRIC CITRATE

Recipe.—Solution of ferric sulfate	42.0 Gm.
Citric acid	15.0 Gm.
Ammonia water	44.0 cc.
Water, a sufficient quantity,	
To make	50.0 Gm.

Mix the ammonia water with 150 cc. of cold water, and the solution of ferric sulfate with 500 cc. of cold water. Add the latter solution slowly to the diluted ammonia water, with constant stirring. Pour the mixture on a wet muslin strainer, and allow the liquid to run off and the precipitate to drain. Then remove the moist mass from the strainer, mix it well with 300 cc. of cold water, again pour it on the strainer, and let it drain. Repeat this washing with several successive portions of cold water in the same manner, until the washings cease to produce more than a slight cloudiness with barium chloride test solution. Then allow the precipitate to drain completely, transfer it to a porcelain capsule, add the citric acid, and heat the mixture, on a water bath, to 60° C. stirring constantly until the precipitate is dissolved. Lastly, filter the liquid, and evaporate it, at the above-mentioned temperature, until it weighs 50 Gm.

Chemical Explanation.—This is substantially the recipe given in N.F. V, except that the Formulary directed that the liquids be measured, not weighed. The first stage of the process of the precipitation of ferric hydroxide from the solution of ferric sulfate is by the following reaction:

Ferric sulfate	plus	Ammonium hydroxide	give	Ferric hydroxide	plus	Ammonium sulfate.
$Fe_2(SO_4)_3$	+	NH_4OH	=		+	

Complete this equation.

The ferric hydroxide is freed from ammonium sulfate by washing with water, and is then treated with citric acid, which converts the moist ferric hydroxide into solution of ferric citrate, viz.:

Ferric hydroxide	plus	Citric acid	give	Ferric citrate	plus	Water.
$Fe(OH)_3$	+	$H_3C_6H_5O_7$	=		+	

Complete this equation.

Calculations.—As the ferric citrate is a rather variable product, containing excess of citric acid, attempts to figure out proportions by molecular weights are of no avail.

Remarks on Process.—*Place the diluted ammonia in a quart fruit jar,* and pour therein the solution of ferric sulfate diluted with 500 cc. of water. Note the red-brown ferric hydroxide precipitates as a magma (p. 167). Note that this is an antidote for arsenic (p. 571).

Pour mixture on wet muslin strainer, spread upon a straining rack. Unless the strainer is of fine mesh, the precipitate will run through. If too fine, the draining will be a slow operation. In large operations it is well to have three strainers on racks placed one above the other, and the magma is poured into the upper one. Most of the precipitate which passes through the upper strainer is caught by the middle one, and whatever does get through the middle one is caught by the lowest one. In laboratory work the laying of a 6-inch filter paper flat on the strainer holds the magma excellently. Collect drippings in pint evaporating dish and return to strainer whatever passes through containing magma. The drippings should be clear and colorless.

Remove mass from strainer while washing. This part of the procedure is a smeary process in the laboratory operation. In large operations, where the strainer is fine duck attached to the frame, the magma can be easily scraped from the strainer with a big spoon; but in the laboratory process it is usually better to wash magma while on the strainer, and that either with a syphon (p. 149) or by continuous washing with inverted flask (p. 148). In washing thus, be careful not to disturb the magma so that it will run through strainer.

Wash until drippings give no precipitate with barium chloride. That is, until free from ammonium sulfate.

Transfer magma to porcelain capsule—that is, to evaporating dish, by scraping off the strainer with spatula or with a spoon.

Do not heat magma and citric acid above 60° C.—that is, even the full heat of a water bath is apt to decompose the citrate.

Filter solution and evaporate in tared pint evaporating dish.

MAKE SCALED FERRIC CITRATE (U.S.P. VIII)

Recipe.—Solution of ferric citrate. .... 25 Gm.

Evaporate the solution on a water bath, at a temperature not exceeding 60° C., to the consistence of syrup, and spread it on plates of glass, so that, when dry, the salt may be obtained in scales.

Keep the product in well-stoppered bottles, protected from light.

Remarks on Process.—Solution of ferric citrate (N.F. V) is about 50 per cent solid ferric citrate, and the 25 Gm. should, therefore, yield about 12.5 Gm. of the scaled salt.

Evaporate at low temperature (60° C.) to avoid decomposition.

Spread syrupy liquid on sheet of glass or on a pill tile. Be sure to spread thinly, using glass rod in getting layer smooth. If poured on thickly, opaque scales result.

Leave liquid on plates until perfectly dry, using no heat whatever. Artificial heat—even a radiator—causes blisters.

If properly prepared, the dry salt will scale off the pill tile without scraping, and that in the form of beautiful shining garnet scales.

Iron and ammonium citrate U.S.P. is made similarly, the only difference being the addition of ammonia water to the solution of ferric citrate before scaling.

THE SCALE SALTS OF IRON

Having discussed the official ferrous and ferric salts, we can now consider the third group of official iron compounds—the scale preparations of iron.

These preparations are not always definite chemicals; thus, the official soluble ferric pyrophosphate is a mixture of pyrophosphate of iron, which in pure form is an insoluble green-gray powder, and sodium citrate, with traces of sodium pyrophosphate and ferric citrate. The scale preparations are bright, shining fragments, which are not crystals, despite an impression to that effect.

Crystals are bodies having definite geometric form, and any examinations of a scale preparation, no matter how superficial, will prove absence of distinct unvarying form. Preparations are scaled just as molasses candy is made—by concentrating to thick syrup and pouring this on a smooth hard surface, usually on sheets of glass.

All scale preparations of iron are made directly or indirectly from ferric hydroxide, that red-brown magma formed by adding solution of ferric sulfate to a diluted water of ammonia.

If we treat the magma with citric acid, ferric citrate is formed; if tartaric acid be the acid added, we get ferric tartrate; while if we use acid potassium tartrate (potassium bitartrate), iron and potassium tartrate will be the product.

The chemistry of these scale preparations of iron has received considerable attention. Belloni believes that ferric citrate represents $[Fe_3(C_6H_5O_7)(OH)_2]_3C_6H_5O_7$ and $[Fe(C_6H_5O_7)_2Fe_2(OH)_4]_3C_6H_5O_7$. Cowley claims that iron and ammonium citrate is a true salt having the formula $(NH_4)_3Fe(C_6H_5O_7)_2$ to which Belloni seems to agree, although he reports exceedingly complex formulas for other forms of ammoniated ferric citrate. Physical chemists emphasize that the scale salts are really colloidal solutions of ferric hydroxide in complex hydroxy-acid groups similar to those suggested by Belloni for ferric citrate. Loeser points out that the colloidal nature of the scale salts makes them less toxic when administered intravenously.

While former Pharmacopœias recognized a number of scale salts of iron (all enumerated below) U.S.P. XI gives official sanction to only two, *iron and ammonium citrate* and *green iron and ammonium citrate*. Since both of these are prepared from scale ferric citrate, the latter will be given first consideration even though it is no longer official.

Ferri Citras (U.S.P. VIII), or *Ferric Citrate*, is made by evaporating a solution of ferric citrate at a temperature not higher than 60° C. to a thin syrup, and then scaling this by pouring it on a glass plate. Its preparation is described in detail above.

Ferric citrate is very soluble in water; its solution, however, takes place quite slowly, as is also true of most of the scale salts of iron.

In dissolving these salts they should never be reduced to powder, nor is it advisable to triturate in a mortar with a solvent. The solution is effected far more rapidly by pouring the scale salts upon the full amount of solvents contained in a bottle and vigorously shaking.

But even thus, the solution of the salt requires considerable patience, hence the use of a solution of ferric citrate is advisable wherever possible. The very fact that ferric citrate and other scale salts slowly dissolve renders them valuable for the manufacture of pills, because, when blended with an excipient, they are apt to retain their form, producing the pills that do not flatten.

Ferric citrate is unstable on exposure to light, liberating carbon dioxide and acetone.

Ferric citrate is a chalybeate tonic and is given in 4-grain doses.

FERRI ET AMMONII CITRATES—Iron and Ammonium Citrates

(Ferr. et Ammon. Cit.—Ferri et Ammonii Citras U.S.P. X)

Iron and Ammonium Citrates contain ferric citrate equivalent to not less than 16.5 per cent and not more than 18.5 per cent of Fe.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Thin, transparent, garnet-red scales; saline, mildly ferruginous taste; somewhat deliquescent; completely soluble in water; insoluble in alcohol; chars on heating, leaving ferric oxide. For details, see U.S.P., p. 162.

For *tests for identity*, for *impurities* (ferric citrate, tartrate) and for *assay*, see U.S.P., p. 162.

Remarks.—Ferric citrate is very slowly soluble in cold water; hence a more soluble form, made by adding ammonia water to solution of ferric citrate and scaling, is the one chosen for inclusion in the Pharmacopœia. It is an interesting fact that while ammonia water precipitates the crystalline ferrous and ferric salts, it simply darkens and renders more soluble the scale preparations.

While ferric citrate occurs in garnet-red scales, the scales of iron and ammonium are yellow brown. Like the other scale salts of iron it is a tonic.

Dose.—2 Gm. (30 grains).

FERRI ET AMMONII CITRATES VIRIDES—Green Iron and Ammonium Citrates

(Ferr. et Ammon. Cit. Virid.)

Green Iron and Ammonium Citrates contain ferric citrate equivalent to not less than 14.5 per cent and not more than 16 per cent of Fe.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Thin, transparent green scales or granules; odorless; saline ferruginous taste; deliquescent; readily soluble in water; insoluble in alcohol. For details, see U.S.P., p. 163.

For *tests for identity*, for *impurities* (same as iron and ammonium citrates) and for *assay*, see U.S.P., p. 163.

Remarks.—This new official scale salt of iron and its related substance, the garnet-red iron and ammonium citrate, are made by the same method except that the red citrate contains as much as 18 per cent of iron whereas the green citrate contains 14.5 to 16 per cent of the metal. The green citrate also contains a larger amount of ammonium citrate than does the red salt and is therefore said to be less painful and less liable to produce coagulation of proteins than will the red citrate when administered intramuscularly or hypodermically. Green iron and ammonium citrate is one of the many forms of iron introduced for the treatment of anemia during the past few years.

Dose.—0.06 Gm. (1 grain) by parenteral injection.

Ferri et Quininæ Citras (U.S.P. IX) or *Iron and Quinine Citrate* is made by adding citric acid and the uncombined alkaloid, quinine, to a solution of soluble ferric citrate, and then scaling the resulting liquid.

This chemical is in transparent deliquescent, greenish or golden-yellow scales that are easily soluble in water.

Iron and quinine citrate, like all the scale salts of iron, is a tonic. *Dose.*—250 mg. (4 grains).

Ferri et Strychninæ Citras (U.S.P. VIII), or *Iron and Strychnine Citrate*, is made by adding a solution of the alkaloid strychnine, in citric acid, to a solution of iron and ammonium citrate.

It is important to note that in making the iron and quinine citrate and iron and strychnine citrate, the uncombined alkaloid is used with the citric acid, and not one of its salts.

By reason of containing the poison strychnine the dose of iron and strychnine citrate is somewhat less than that of the other scale salts, being about 2 grains.

Ferri Phosphas Solubilis (U.S.P. X N.F. VI) or *Soluble Ferric Phosphate.* This is ferric phosphate rendered soluble by the presence of sodium citrate. While no recipe is given in the Formulary, for the manufacture of this salt, the Pharmacopœia of 1890 directed that it be made by mixing solution of ferric citrate with a solution of sodium phosphate and then scaling the resulting fluid.

Ferric phosphate in the pure form is insoluble, but the mixed product resulting from the combination of ferric phosphate with alkaline citrates is soluble. Hence this official is not a definite compound but is a mixture of sodium citrate with ferric phosphate and may be called sodioferric citrophosphate. The soluble phosphate is decomposed upon prolonged exposure to light, hence its solutions should be kept in amber-colored bottles. It is highly esteemed as a tonic.

Dose.—250 mg. (4 grains).

Ferri Pyrophosphas (N.F. VI), or *Soluble Ferric Pyrophosphate*, is an indefinite mixture of sodium citrate with ferric pyrophosphate. It should contain not less than 10.5 per cent of metallic iron and is used as a tonic in 4-grain doses.

Ferri et Ammonii Tartras (U.S.P. VIII), or *Iron and Ammonium Tartrate*, is prepared by adding ferric hydroxide to a solution of ammonium tartrate and tartaric acid, evaporating to syrupy consistence, and pouring on plates of glass. As the last part of the process—evaporating and pouring on plates of glass—is common to all scale preparations, we will, for brevity's sake, call it in future *scaling.* Like all other scaled iron salts, the product is a tonic. Its dose is 4 grains.

Ferri et Potassii Tartras (U.S.P. VIII), or *Iron and Potassium Tartrate*, is prepared like iron and ammonium tartrate. In the latter the ferric hydroxide is treated with what may be considered a solution of ammonium bitartrate, whereas in the iron and potassium tartrate the magma is dissolved by treating with potassium bitartrate or cream of tartar. This fact is worth passing notice, inasmuch as it clearly shows that acid salts possess acid properties; that is, that the hydrogen found in acid salt is capable of combining with a metal, just as does the hydrogen with the acid from which it is derived.

A commercial form of iron and potassium tartrate formerly enjoyed large popularity. This was the chemical in the form of an oval lump, to one end of which was attached a loop of string or ribbon. This form was formerly highly esteemed in France under the name of "*boule de Mars.*" This name, by the way, suggested the alchemistic title of the element iron, which was called, by the forerunners of chemistry, after the god of war, Mars. The "*boule de Mars*" was supposed to be carried around by the patient, and when a chalybeate tonic was desired, the lump was suspended into a glass of water or wine, and after sufficient immersion it was supposed that enough of the chemical would be dissolved in the fluid, thus producing a pleasant tonic.

Iron and potassium tartrate is used as a tonic, in 4-grain doses.

BIBLIOGRAPHY

Iron.—(Sources) Woehler, A., 163, 1872, 247; Nitze, Jl. Soc. Ch. Ind., 11, 1892, 246; Anon., Jl. Soc. Ch. Ind., 23, 1904, 917; Anon., Jl. Ind. Eng. Ch., News Ed., 7, Sept., 20, 1929, 8. (History) Geike, Prehistoric Europe, 1881, 6; Knott, N. Y. Med. Jl., 88, 1908, 919, 969 and 1029; Balaiew, Metallurgie, 8, 1911, 449 and 699; Hackh, A.J.P., 90, 1918, 490; Friend, Jl. Soc. Ch. Ind., 44, 1925, 388; Hadfield, *ibid.*, 44, 1925, 1029; Garland and Bannister, *ibid.*, 46, 1927, 648; Mathews, C.A., 21, 1927, 1763; Bone, J. Soc. Ch. Ind., 47, 1928, 932; Krasa, C.A., 26, 1932, 399; Campbell and Thum, C.A., 26, 1932, 403. (Production) Larke, Jl. Soc. Ch. Ind., 44, 1925, 310; Bone, *ibid.*, 51, 1932, 311; Anon., *ibid.*, 51, 1932, 185.

Iron Manufacture.—(Cast iron) Gayley, Jl. Ind. Eng. Ch., 5, 1913, 241; Johnson, Met. Ch. Eng., 13, 1915, 161, 227, 373, 429 and 497; *ibid.*, 14, 1916, 38, 77 and 591; Moerck, 95, 1923, 515. (Wrought iron) Anon., Jl. Soc. Ch. Ind., 19, 1900, 1116. (Bessemer steel) Bessemer, Eng. pat. 2768, Dec. 7, 1855, through Roscoe and Schorlemmer, 2, 1880, 69; Robertson, Jl. Soc. Ch. Ind., 43, 1924, 804; Holland, Jl. Frank. Inst., 208, 1929, 695. (Thomas and Gilchrist process) Lindsey, C.A., 5, 1911, 1487. (Heroult steel) Richards, Met. Ch. Eng., 8, 1910, 563; Greene, C.A., 23, 1929, 1059. (Vanadium steel) Anon., Foundry, 37, 1911, 137; Karr, Brass World, 8, 1912, 274. (Manganese steel) Hadfield, Jl. Soc. Ch. Ind., 44, 1925, 1029. (Chrome steel) Bellinger, C.A., 25, 1931, 560.

Iron Therapy.—Clark, Ph. Jl., 128, 1932, 490 and 511; 129, 1932, 2 and 22; Fischer, *ibid.*, 129, 1932, 290; Moller C.A., 26, 1932, 257.

Steel.—(Classification) Richards, Met. Ch. Eng., 10, 1912, 265. (As iron carbide) Ruff, Metallurgie, 8, 1911, 456 and 497.

Cast Iron.—(Properties) Marx, A.J.P., 6, 1834, 84.

Tantiron.—Carnell, Ch. News, 116, 1917, 92; Anon., C.A., 12, 1918, 2309.

Stainless Steel.—Daeves and Mussat, C.A., 16, 1922, 3852; Hatfield, Jl. Soc. Ch. Ind., 42, 1923, 99; Blumenschein, Jl. A.Ph.A., 12, 1923, 248; Hadfield, C.A., 10, 1916, 1161; Jl. Soc. Ch. Ind., 45, 1926, 168 and 49, 1930, 41T; Parmiter, C.A., 18, 1924, 3348; Hatfield, Jl. Soc. Ch. Ind., 42, 1923, 99; C.A., 19, 1925, 2018; J. Soc. Ch. Ind., 45, 1926, 568 and 48, 1929, 1060; Primrose, C.A., 21, 1927, 1956; Kroll, Jl. Soc. Ch. Ch. Ind., 48, 1929, 723B; Brophy, C.A., 23, 1929, 805; Kawakami, C.A., 23, 1929, 2139 and 4916; Sergeson, C.A., 23, 1929, 1853; Mitchell, C.A., 23, 1929, 2919; Bain, Jl. Soc. Ch. Ind., 51, 1932, 662 and 683.

Invar.—Guillaume, Jl. Soc. Ch. Ind , 48, 1929, 41.

Elinvar.—Shubrooks, C.A., 26, 1932, 2680.

Iron Inks.—(History) Martell, Schw. Ap. Zt., 53, 1915, 390 and 403; Vanino, Arch. Pharm., 253, 1915, 505.

Iron Ferrocyanides.—Muller and Treadwell, Jl. prakt. Ch., 80, 1909, 170.

Iron Thiocyanate.—Bailey, C.A., 22, 1928, 199.

Reduced Iron.—Creuse, A.Ph.A., 22, 1874, 435; LaWall and Harrison, Jl. A.Ph.A., 8, 1919, 811.

Ferrous Carbonate.—Boudet, Ph. Jl., 1, 1841, 70; Vanino, Arch. d. Pharm., 251, 1913, 294; Baudisch and Weld, C.A., 19, 1925, 3182.

Vallet's Mass.—Vallet, Jl. de ph., 24, 1838, 289; Humphrey, Ph. Jl., 70, 1903, 643.

Blaud's Pills.—(History) Boudet, Ph. Jl., 1, 1814, 70; Ince, P., Jl., [3], 25, 1894, 131; Lemaire, A.Ph.A , 57, 1909, 94. (Preservation) Leubner, Merck's Rep., 19, 1910, 31; Lang, C.A., 24, 1930, 5110 and C.A., 25, 1931, 1638.

Griffith's Mixture.—Griffith, A.J.P., 5, 1834, 35; Ince, Ph. Jl., 1, 1841, 248.

Fluid Ferrous Carbonate.—Wilbert, A.J.P., 79, 1907, 525.

Syrup of Ferrous Iodide.—(History) Mowry, A.J.P., 58, 1886, 289. (Manufacture and properties) Judge, A.J.P., 48, 1876, 157; Alpers, Jl. A.Ph.A., 3, 1914, 420; Toplis, A.Ph.A., 58, 1910, 1258; Thum, Am. Dr., 57, 1910, 130; Haussmann, A.J.P., 72, 1900, 217; Dupasquier, Jl. de ph., 27, 1841, 117; Couch, Ph. Jl., 115, 1925, 687; Husa and Klotz, Jl. A.Ph.A., 23, 1934, 679. (Stability) Arny and co-workers, Jl. A.Ph.A., 18, 1929, 265 and 384; *ibid.*, 20, 1931, 1156 and A.J.P., 103, 1931, 504; Becker and Berg, Jl. A.Ph.A., 18, 1929, 503. (Therapeutics) Hommell, Pract. Dr., 49, Mch., 1931, 15.

Pills of Ferrous Iodide.—Anon., A.J.P., 29, 1857, 87.

Ferrous Lactate.—Gerves, Arch. d. Pharm., 163, 1863, 103.

Ferrous Sulfate.—(History) Arny, Am. Dr., 34, 1901, 3. (Granulated) Trimble, A.Ph.A., 36, 1888, 140.

Ferric Chloride.—(Structure) Grünewald and Meyer, B., 21, 1888, 687; Friedel and Crafts, Comp. rend., 106, 1888, 1764 and 107, 1888, 301; Jufereo, Zt. anorg. Ch., 59, 1908, 82. (Solubility in ether) Rothe, Jl. Soc. Ch. Ind., 11, 1892, 940. (Medical uses) Hanzlik, Jl. A.M.A., 72, 1919, 577.

Tincture of Ferric Chloride.—Squibb, A.J.P., 29, 1857, 289; Rother, A.J.P., 56, 1884, 407.

Tincture of Citrochloride of Iron.—Cruse, Dr. Circ., 17, 1873, 89; Ruddiman, Pharm. Era, 42, 1909, 622; Nichols, Jl. A.Ph.A., 13, 1924, 38.

Bestuscheff's Tincture.—Mansoau, Nat. Dr., 40, 1910, 525.

Ferric Hypophosphite.—Weinland and Hieber, C.A., 14, 1920, 157.

Ferric Sulfates.—(Composition) Recoura, Ann. chim. phys., [8], 11, 1907, 263 and Comp. rend., 153, 1911, 1223.

Monsel's Solution.—Wilbert, Am. Dr., 43, 1903, 202; Monsel, Jl. de ph. et ch., 32, 1857, 208.

Ferric Hydroxide.—Bancroft, C.A., 9, 1915, 1437.

Arsenic Antidote.—Bunsen, Jl. de ph., 20, 1834, 567; Raubenheimer, Jl. A.Ph.A., 2, 1913, 529; England, A.J.P., 87, 1915, 59; Wood, Jl. A.Ph.A., 12, 1923, 482; Hogstad, N.W. Dr., 34, May, 1926, 60; Boutaric and Perreau, C.A., 22, 1928, 2502; Yeo, Jl. Am. Ch. Soc., 52, 1930, 2785.

Dialyzed Iron.—Graham, Ch. News, 4, 1861, 87; Maisch, A.J.P., 49, 1877, 342; Trimble, A.J.P., 50, 1878, 60; Fischer, C.A., 4, 1910, 3253; Smith and Giesy, Jl. A.Ph.A., 12, 1923, 855; Slater, Jl. Soc. Ch. Ind., 44, 1925, 501T; Polson, C.A., 22, 1928, 4651; Sorum, Jl. Am. Ch. Soc., 50, 1928, 1263 and 51, 1929, 1155; Jablczynski and Emin, C.A., 26, 1932, 3167; Nichols and co-workers, C.A., 26, 1932, 1497.

Saccharated Ferric Oxide.—Mannich and Rojahn, Ber. d. Pharm. Ges., 32, 1922, 158.

Basham's Mixture.—(History) England, A.J.P., 75, 1903, 383; Cooper, Spatula, 27, 1920, 7. (Manufacture) Beral, A.J.P., 4, 1883, 64. (Deterioration) Husa and Birmingham, Jl. A.Ph.A., 22, 1933, 495.

Scaled Salts of Iron.—Rieckher, Jahrbuch Pharm., 40, 1873, 65 and 134; Power, Ph. Rund., 9, 1891, 205; Pickering, C.A., 7, 1913, 3487; Ferrey, C.A., 23, 1929, 1469; Loeser, Jl A.Ph.A., 18, 1929, 124; Friede, Ap. Zt., 45, 1930, 161; Morton, Quart. Jl. Ph., 4, 1931, 459; Franke, C.A., 25, 1931, 5145; Harrar and Germann, C.A., 26, 1932, 1540.

Boule de Mars.—Duhamel, A.J.P., 14, 1842, 224.

Iron and Potassium Tartrate.—Klie, A.J.P., 48, 1876, 170.

Iron and Ammonium Citrate.—Cowley, Ph. Jl., 86, 1911, 1313.

Ferric Citrate.—Duhamel, A.J.P., 14, 1842, 225; Stevens, A.Ph.A., 55, 1907, 153; Belloni, C.A., 15, 1921, 839; Siboni, C.A., 24, 1930, 4509. (Deterioration) Fry and Gerwe, Jl. Ind. Eng. Ch., 20, 1928, 1392; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1153.

Iron and Strychnine Citrate.—O'Connor, A.J.P., 30, 1858, 275.

Ferric Phosphate.—Maisch, A.J.P., 31, 1859, 410; Heydenreich, A.J.P., 33, 1861, 294; Mueller, Jl. A.Ph.A., 11, 1922, 787.

Ferric Pyrophosphate.—Heydenreich, A.J.P., 33, 1861, 294; Robiquet, A.J.P., 29, 1857, 401; Maisch, A.J.P., 31, 1859, 410.

CHAPTER XXXII

ARSENIC, ANTIMONY, TIN, GOLD, AND PLATINUM

ARSENIC

Symbol, As. Atomic weight, approximately 75

THE chief ores from which this element is derived are *realgar*, As_2S_2, *orpiment*, As_2S_3; the latter word, a corruption of "auri pigmentum," which, translated, means the color of gold or of fire, so-called because of its brilliant yellow tint. Another ore of arsenic—*flowers of arsenic* or *white arsenic*—As_2O_3, is mined in certain districts of Styria, where the natives become habituated to its use and are immune from its poisonous action. This immunity, according to Schwartze, is not due to habituation but to the fact that solid arsenic is so slowly soluble as to be almost inert. (See p. 581.)

Arsenic has been known from comparatively early times. The red and yellow sulfides were known to the Greek and Roman writers. The white arsenic appears to have been known to Geber in the eighth century. In the eleventh century Avicenna differentiated between the white arsenic and the red and yellow. Albertus Magnus, in the thirteenth century, appears to have isolated the element, and the practical separation was a matter of technic in the seventeenth century.

The word arsenic is derived from the Greek word *arsenikon,* which was the term used to designate the ore, orpiment. The *metallurgy* of arsenic is somewhat similar to that of the other elements which we have considered, it being isolated by heating the oxide with coal, as shown in the following equation:

$$As_2O_3 + C_2 = As_2 + CO + CO_2.$$

This process is not used much now, since native arsenic oxide is comparatively rare, and most of the element is made by heating arsenical iron, and from mispickel, when arsenic is freed and sublimes. The respective reactions are:

$$\begin{aligned} Fe_3As_4 &+ \text{heat} = Fe_3As_2 + As_2 \\ Fe_2As_2S_2 &+ \text{heat} = 2FeS + As_2. \end{aligned}$$

Metallic arsenic occurs in the form of crystalline masses, which are steel gray when freshly sublimed, but becoming dull and black on exposure to air. Besides this crystalline form, amorphous forms are known.

Arsenic and antimony, like zinc and aluminum, form a group about midway between the metals and the nonmetals, and the nonmetallic character of arsenic and antimony is even more strikingly demonstrated than in the case of zinc and aluminum. In fact, the most abundant compound of arsenic is one in which arsenic shows its negative character, namely, in arsenic trioxide (arsenous acid, U.S.P. 1890). But, while showing many points in common with the nonmetallic elements, its metallic properties are well defined. Thus, it is precipitated with hydrogen sulfide, as are the other metals of this group, and combines with acids to form the salts of arsenic, such as arsenic chloride and arsenic iodide.

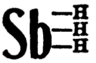
On the other hand, when combined with alkalis the negative side is clearly demonstrated, and among the official compounds we find solution of potassium arsenite and sodium arsenate.

The **tests** for arsenic are as follows: the yellow sulfide (orpiment), produced when hydrogen sulfide is passed through an acidulated solution of arsenous acid. Silver nitrate test solution produces a yellow precipitate of silver arsenite or a brown precipitate of silver arsenate, according to the valence of the arsenic in the suspected solution. A characteristic test for arsenic is the so-called *cacodyl reaction,* which is brought about by fusing the arsenic with potassium or sodium acetate, when a disgusting odor of cacodyl is produced. For details descriptive of this organic compound, see p. 670. The equation is:

$$As_2O_3 + 4KC_2H_3O_2 = [As(CH_3)_2]_2O + 2K_2CO_3 + 2CO_2.$$

Compounds of arsenic, treated with copper sulfate and ammonia, yield a characteristic green precipitate of copper arsenite. This green insoluble substance was formerly largely used in the technic under the name of *Scheele's green*, as a coloring matter. The danger of this body however, has caused it to fall more or less into disuse.

Arsenic was formerly largely employed by poisoners, and accordingly many tests have been devised for the detection of the element, such as the tests suggested by Marsh, Fleitmann, Gutzeit, and Reinsch. The principle of action of the first three of these is based on the formation of the gas, hydrogen arsenide, AsH_3, which is produced by the union of hydrogen (generated by action of sulfuric acid on zinc), with arsenic in the suspected substance, forming hydrogen arsenide, AsH_3, which is analogous to ammonia, NH_3; to phosphine (phosphoretted hydrogen, PH_3), that spontaneously combustible gas mentioned on p. 433, and to antimoniuretted hydrogen (stibine, SbH_3), mentioned a little further along. These four gases can best be compared in tabulated form:

Nitrogen,	valence III	gives ammonia,	NH_3,	graphically	
Phosphorus,	"	III "	phosphine,	PH_3,	"	
Arsenic,	"	III "	arsine,	AsH_3,	"	
Antimony,	"	III "	stibine,	SbH_3,	"	

Hydrogen burns to pure water ($H_2 + O = H_2O$), while AsH_3, in burning, yields water and metallic arsenic ($2AsH_3 + 3O = 3H_2O + As_2$); the latter separates as an arsenic spot on a piece of porcelain, just as the carbon in gas separates as soot when burned in a fish-tail burner. The details of Marsh's test are beyond the limits of this work, and the reader is referred to one of the books on analytic chemistry mentioned in the preface.

Mention, however, must be made of the fact that antimony compounds treated with nascent hydrogen produced from zinc and sulfuric acid form antimoniuretted hydrogen, SbH_3, which, on burning, likewise deposits a stain on a porcelain dish. This latter stain is, however, brown black, and is not soluble in Labarraque's solution, as is the arsenic spot. Marsh's test is no longer given in the Pharmacopœia, being replaced by a modification which does away with the cumbersome apparatus used in Marsh's test. This modification is *Gutzeit's test*, in which the hydrogen is developed from zinc and sulfuric acid in a test tube, and the suspected substance added. If arseniuretted hydrogen forms, it turns a strip of mercuric bromide test paper yellow or brown according to the amount of AsH_3 obtained from the sample.

Reinsch's test is produced by placing a sheet of bright metallic copper into the suspected solution. If arsenic be present, an electrolytic action takes place, with the deposition of that element on the copper plate, which accordingly becomes blackened. *Bettendorf's test* consists in dissolving arsenic in concentrated hydrochloric acid, adding solution of stannous chloride, and introducing into the test tube containing this mixture a piece of tin foil. If arsenic be present, a brown coloration takes place. This is of particular value in testing bismuth compounds for arsenic.

In experimenting with Marsh's test, the operator should be careful regarding the inhaling of the vapors produced, as the hydrogen arsenide vapors are very poisonous, the chemist Gehlen having been killed by this substance during experiments in 1815. It has been noted that wall-paper colored green by the use of Scheele's green produces symptoms of arsenical poisoning in persons in the room. This is due to the generation of AsH_3 by microscopic plants (molds) that develop on moist wall paper.

Arsenic, like nitrogen and phosphorus, exhibits the valence III and V, as shown in two oxides—As_2O_3 and As_2O_5—which are called arsenous and arsenic oxides respectively.

The official preparations of arsenic are:

Arsenic trioxide. At least 99.8 per cent absolute As_2O_3.

Solution of arsenous acid, containing from 0.975 to 1.025 per cent arsenic trioxide.

Solution of potassium arsenite, containing from 0.950 to 1.050 per cent arsenic trioxide.

Arsenic triiodide. At least 99 per cent AsI_3.

Solution of arsenous and mercuric iodides (N.F. VI), containing from 0.95 to 1.05 each of arsenous iodide and of mercuric iodide.

ARSENI TRIOXIDUM—Arsenic Trioxide

(**Arsen. Trioxid.**—Arsenous Acid, Arsenous Oxide)

As_2O_3. Molecular weight, 197.82

Arsenic Trioxide, when dried to constant weight at 100° C., contains not less than 99.8 per cent of As_2O_3.

Summarized Description.

Opaque, white powder, or amorphous, transparent, glasslike masses, or crystalline, opaque, porcelain-like masses; in moist air the glassy variety changes to the opaque; soluble in water (glassy variety more than the crystalline) and in glycerin; slightly soluble in alcohol and ether; soluble in hydrochloric acid and in alkaline solutions; volatilizes on heating, subliming to transparent octahedral crystals; heated with charcoal, in a tube metallic arsenic sublimes and deposits as a mirror. For details, see U.S.P., p. 72.

For *tests for identity*, for *impurities* (antimony, tin, cadmium) and for *assay*, see U.S.P., p. 73.

Remarks.—This most important of the official arsenical preparations, called arsenous acid by the Pharmacopœia of 1890, is more properly termed arsenic trioxide by U.S.P. XI, since it is the anhydride As_2O_3, the true acid being produced only when the official substance is dissolved in water:

$$As_2O_3 + 3H_2O = 2H_3AsO_3.$$

Hence the aqueous solution still retains as official name the phrase, *liquor acidi arsenosi*.

Arsenic trioxide is prepared by the roasting of arsenical ores, when the oxide which is formed sublimes and is caught in appropriate condensing chambers. It is then purified by resublimation.

Arsenic trioxide acts as a reducing agent, being oxidized by potassium permanganate, and converting iodine into hydriodic acid. This explains the volumetric estimation of the chemical by means of a decinormal iodine solution. (See p. 1011.) A volumetric determination of the chemical can also be effected by use of decinormal permanganate solution.

Arsenous acid is a valuable alterative. Applied in the form of a powder, it acts as an escharotic, and for this purpose was formerly employed for the dusting of cancerous growths. Its action in this way, however, was dangerous, and at present it is rarely so used.

Arsenic chiefly in the form of lead arsenate is largely used by spraying for the destruction of fruit tree pests. The fruit thus sprayed must be carefully washed or arsenical poisoning is apt to result.

Many of the largely advertised rat poisons consist of arsenous oxide, either free or admixed. When reduced to colloidal form arsenic trioxide kills rats with much greater rapidity than when in its usual degree of fineness. The antidote for such nostrums is, therefore, the same as that for arsenous oxide, namely, ferric hydroxide or ferric hydroxide with magnesia. (See p. 572.)

Dose.—2 mg. (1/30 grain).

LIQUOR ACIDI ARSENOSI—Solution of Arsenous Acid

For recipe see p. 209.

This is a 1 per cent aqueous solution of arsenic trioxide, containing a sufficient quantity of hydrochloric acid to insure a complete solution. In the Pharmacopœia of 1870 it was styled the *solution of arsenous chloride*, but investigations have shown that the hydrochloric acid, in this case, acts merely as a solvent, not converting the oxide into chloride.

Dose.—0.2 cc. (3 minims).

LIQUOR POTASSII ARSENITIS—Solution of Potassium Arsenite

(**Liq. Pot. Arsen.**—Fowler's Solution, Liquor arsenicalis seu Fowleri, P.I.)

Solution of Potassium Arsenite contains, in each 100 cc. the equivalent of not less than 0.950 Gm. and not more than 1.050 Gm. of As_2O_3.

Condensed Recipe.

Boil 10 Gm. arsenic trioxide and 7.6 Gm. potassium bicarbonate in a flask with 100 cc. distilled water until the solids are dissolved. Then add enough distilled water to make 950 cc. and 30 cc. alcohol and, finally, add enough distilled water to make 1000 cc. For details see U.S.P., p. 219.

Summarized Description.

Clear or faintly opalescent liquid having an alkaline reaction. For details, see U.S.P., p. 219.

For *tests for identity*, for *impurities* (arsenate) and for *assay*, see U.S.P., p. 219.

Remarks.—This preparation, commonly called "Fowler's solution," is made from arsenic trioxide and potassium bicarbonate. The omission of compound tincture of lavender in the eleventh revision does not improve the preparation. It contains 1 per cent of arsenic trioxide.

The equation for its manufacture is either—

$$4KHCO_3 + As_2O_3 + 3H_2O = 2K_2HAsO_3 + 4H_2O + 4CO_2$$

or

$$2KHCO_3 + As_2O_3 = 2KAsO_2 + 2CO_2 + H_2O.$$

The Pharmacopœia directs that the potassium bicarbonate and the arsenic trioxide be boiled together in water to insure chemical combination. If a solution of potassium bicarbonate and a solution of arsenic trioxide are mixed together in the cold, no reaction takes place, and, in fact, some authorities claim that even boiling produces but a slight effect on the two constituents. How little decomposition occurs is shown by the fact even when twice the amount of arsenous acid is boiled with solution of potassium bicarbonate, and even when such solution is evaporated to dryness and then redissolved in water, the latter liquid still effervesces with acids. Despite this fact, some authorities claim that a meta-arsenite of potassium ($KAsO_2$) is produced; while others hold to the ortho-arsenite formula, K_2HAsO_3; this is supposedly the acid potassium salt of H_3AsO_3.

It will be noted that while former Pharmacopœias directed that Fowler's solution should contain 1 per cent by weight of arsenic trioxide, U.S.P. XI directs a weight-volume solution; that is, 1 Gm. As_2O_3 to 100 cc.

Fowler's solution is one of the most popular of arsenical preparations, being particularly esteemed as an alterative in cases of malaria. Many physicians in malarial countries consider this preparation almost in the light of a specific.

Dose.—0.2 cc. (3 minims).

ARSENI TRIIODIDUM—Arsenic Triiodide

(**Arsen. Triiodid.**—Arseni Iodidum U.S.P. X, Arsenous Iodide)

AsI_3. Molecular weight, 455.67

Arsenic Triiodide, when dried to constant weight over sulfuric acid, contains not less than 99 per cent of AsI_3.

Storage.—Preserve in glass-stoppered bottles, in a cool place and protected from light.

Summarized Description.

Orange-red, crystalline powder; stable when kept cool and protected from light; soluble in about 12 parts of water and in about 28 parts of alcohol; also soluble in chloroform, ether and carbon disulfide; does not lose iodine at water-bath heat, but volatilizes at higher temperatures; liberates iodine and nitrogen oxides when treated with nitric acid; fresh aqueous solution is colorless, but it turns yellow on standing. For details, see U.S.P., p. 72.

For *tests for identity*, and for *assay*, see U.S.P., p. 72.

Remarks.—This compound was formerly made by fusing molecular quantities of metallic arsenic and iodine into a test tube and pouring the fused mass on a slab in order to permit it to solidify. This process, however, was very wasteful of the iodine, and therefore a much better method is by making a solution of iodine in carbon disulfide, and sprinkling therein finely powdered arsenic until the purple color is discharged.

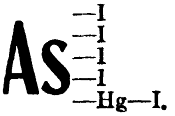
Arsenic iodide is a comparatively unstable compound, losing its iodine by volatilization until its composition is very largely changed. It is, therefore, at its best a rather uncertain preparation, as is the case with sulfur iodide.

This substance is used as an alterative.

Dose.—5 mg. (1/12 grain).

Liquor Arseni et Hydrargyri Iodidorum (U.S.P. X; N.F. VI), or *Donovan's Solution*, after the originator, contains 1 per cent of arsenic triiodide and 1 per cent of mercuric iodide.

Langenhan points out that "the chemistry of Donovan's solution is by no means as simple as is assumed by the textbooks." He even points out the possibility of the formation of a double iodide of arsenic and mercury of a formula something like this



$$\mathrm{As}\begin{array}{l}-\mathrm{I}\\-\mathrm{I}\\-\mathrm{I}\\-\mathrm{I}\\-\mathrm{Hg}-\mathrm{I.}\end{array}$$

The solution should be practically colorless. On standing, it assumes a reddish tint, and such a reddened Donovan's solution should not be dispensed. While some writers claim that the reddening is due to separation of free iodine, Huskisson points out that reddened solutions do not give the iodine reaction with starch paste. The change in color can be largely obviated by keeping a globule of mercury in the solution; taking care to dispense only the clear supernatant fluid.

Recently there has been considerable study of this important but unstable preparation. Husa's findings may be summarized as follows:

1. It is in truth a solution of arsenous acid, hydriodic acid, and hydrogen mercuric iodide.
2. The hydrolysis equations are

$$AsI_3 + 3H_2O = H_3AsO_3 + 3HI,$$
$$HgI_2 + 2HI = H_2HgI_4.$$

3. It could best be prepared by blending proper proportions of arsenous oxide, mercuric iodide, potassium iodide, diluted hydrochloric acid, potassium hydroxide (to neutralize) and water.

4. The above combination yields a far more stable product than that made by the recipe of U.S.P. X.

5. The solution can be best preserved by (*a*) storing in amber bottles; (*b*) using proper stabilizers such as hypophosphorous acid or terpin hydrate.

6. Careful adjustment of the *p*H of the solution (between 6.5 and 7.5). This is attained extemporaneously by the following recipe: arsenous iodide and mercuric iodide, of each 10 Gm.; sodium bicarbonate, 9 Gm.; distilled water to make 1000 cc. This is substantially the recipe of N.F. VI.

Donovan's solution is used as an alterative and tonic.

Dose.—0.1 cc. (1½ minims).

Sodii Arsenas (N.F. V), or *Sodium Arsenate*, $Na_2HAsO_4.7H_2O$, is made by adding arsenous acid to the mixture of sodium carbonate (or sodium hydroxide) and sodium nitrate, and heating same to redness and pouring out the fused mass on a slab, and treating it with boiling water as soon as solidified. The solution is then evaporated until crystallization takes place; the crystals are removed from the mother liquid and dried according to the usual method.

This process furnishes an interesting example of oxidation. Arsenic has the valence III and V, and the two oxides, As_2O_3 and As_2O_5, when treated with water, yield respectively the true arsenous acid (H_3AsO_3) and arsenic acid (H_3AsO_4), the latter being analogous to phosphoric acid, H_3PO_4. (See p. 396.) An arsenate is a salt of arsenic acid, and if we treat sodium carbonate with arsenous acid (which is common, while arsenic acid is rare), we would not get an arsenate, but an arsenite, just as we did in Fowler's solution.

It will be noticed that the arsenical ingredient used above is arsen*ous* oxide (As_2O_3). We have already learned (p. 396) that "ous" acids give "ite" salts, a proof of which, with the very acid we are now considering, is shown in Fowler's solution—liquor potassii arsenitis—where we see that arsenous acid, cooked with potassium bicarbonate, yields potassium arsen*ite*—not the arsen*ate*—shown in equation "a" given on p. 582.

In exactly similar manner sodium carbonate and arsenous acid yield Na_2HAsO_3, sodium arsen*ite*. Necessary to form the arsen*ate* is arsen*ic* acid, As_2O_5 or H_3AsO_4, and, accordingly, if we start out with arsenous acid, it must be oxidized to arsenic acid before the arsenate can be formed. It may be recalled that in making sulfuric acid, sulfur*ous* oxide, SO_2, was oxidized to sulfur*ic* oxide, SO_3, and that the oxidation was accomplished by nitric acid. In oxidizing arsenous oxide to arsenic oxide in the manufacture of sodium arsenate, nitric acid is not adapted, since it, rather than the arsenic preparation, would react with the sodium carbonate, the final product being a mixture of sodium nitrate and arsenic acid; hence we employ sodium nitrate, $NaNO_3$, which at a high heat splits in a manner akin to nitric acid itself, with the liberation of oxygen.

The usually accepted equation of manufacture—

$$(a)\ Na_2CO_3 + As_2O_3 + 2NaNO_3 = Na_4As_2O_7 + N_2O_3 + CO_2,$$
$$(b)\ Na_4As_2O_7 + H_2O = 2Na_2HAsO_4,$$

is more complex than the explanation just given, because of the presence of an intermediate product, sodium pyroarsenate, $Na_4As_2O_7$. This body, however, is analogous to sodium pyrophosphate, $Na_4P_2O_7$, the latter a salt of pyrophosphoric acid, $H_4P_2O_7$, the chemistry of which was explained on p. 496.

Sodium arsenate occurs in colorless transparent prisms, is very poisonous and is soluble in about 1.5 parts of water. It is used as an alterative and tonic in 5-mg. doses.

Sodii Arsenas Exsiccatus (N.F. VI), or *Exsiccated Sodium Arsenate*, is made by driving off the 7 molecules of water of crystallization from the crystalline sodium arsenate by use of a temperature of 150° C.

It is used for making the *solution of sodium arsenate* (N.F. VI). While the exsiccated salt was not recognized by the Pharmacopœia of 1890, the solution of sodium arsenate of that Pharmacopœia was prepared by first exsiccating the crystallized salt, experience showing that when that solution is prepared from the crystalline salt, it is of uncertain strength, since the crystals are usually more or less efflorescent. *Dose.*—3 mg. ($\frac{1}{20}$ grain).

Liquor Sodii Arsenatis (N.F. V) is a 1 per cent solution of exsiccated sodium arsenate (see p. 214).

Liquor Sodii Arsenatis Dilutus (N.F. V). This solution, familiarly called *Pearson's Solution* (see p. 214) is only one tenth the strength of the official solution of sodium arsenate.

Liquor Arsenicalis, Clemens (N.F. IV), or *Clemens' Solution of Arsenic*, is a solution of potassium arsenate and bromide, made by boiling together arsenic trioxide, potassium carbonate and water and then adding bromine to the cooled and diluted solution. It represents about 1 per cent As_2O_3.

ANTIMONY

Symbol, Sb. Atomic weight, approximately 120

This element is sometimes found native in uncombined form, but its chief ore is the sulfide—Sb_2S_3—which is called stibnite.

The symbol Sb as applied to antimony is derived from the Latin name of the element, *stibium*, which is in turn derived from the Greek word *stibi*, which was the name applied to that native sulfide, which has been known since classic times. The etymology of the word antimony has been explained by a curious fable, which relates that Basel Valentine, a monk of the monastery of Erfurt, experimented with the salts of this element on his brother monks, with fatal results, whereupon he named the element *antimoine*—against monks. This theory of the origin of the name, however, has been exploded since the word antimonium was used in a book of Constantine of Salerno (A. D. 1100), and merciless critics have even denied the existence of such a man as Basel Valentine. Suffice it to say that there appeared during the fifteenth century a book entitled "The Triumphant Chariot of Antimony," purported to have been printed from the manuscript of this monk Basel Valentine. It was through the publication of this work that the use of antimony in medicine became popularized. In the sixteenth and seventeenth centuries antimony and its compounds were among the most popular of medicines, the element being isolated by Boerhave. One of the applications of this substance was in the form of a cup made of this metal (*pocula emetica*). Acid or wine was allowed to stand in this cup until a certain amount of this metal had been dissolved. The wine, when drunk, then acted as an emetic. Under the name of "*pilulæ perpetuæ*" small globules of the metal were used in the seventeenth century, enough of the metal being dissolved from the swallowed pill by the acid juices of the stomach to produce the desired effect. The pill, voided either by emesis or through the bowels, was then saved for the next need.

The metallurgy of antimony is accomplished by heating the sulfide with metallic iron, as shown in the following equation:

$$Sb_2S_3 + Fe_3 = 3FeS + Sb_2.$$

In order to facilitate the separation of the metal from the ferrous sulfide a mixture of exsiccated sodium sulfate and coal is added for the purpose of forming a slag with the ferrous sulfide.

Antimony is a brilliant brittle metal, of lamellated texture, and silvery white when chemically pure. The commercial antimony, however, is usually of a bluish-white tint. Antimony is a constituent of several valuable alloys. Thus, *type metal* is a combination of 15 per cent of antimony and 85 per cent of lead; while *pewter* consists of 10 per cent of antimony, 86 per cent of tin, 3 per cent of zinc, and 1 per cent of copper.

The *tests* for antimony are as follows: hydrogen sulfide precipitates from acid solutions of antimony golden yellow (orange) antimony sulfide which, like the sulfides of arsenic, tin, gold, and platinum, will dissolve in ammonium sulfhydrate solution. If, into an acid solution of antimony is placed zinc and platinum in the form of plates, an electrolytic action takes place with the deposition of antimony on the platinum as a black spot. This black spot is soluble in a solution of potassium permanganate.

As mentioned under Arsenic, Marsh's test can be used for the detection of antimony. In fact, the two elements act so similarly when subjected to Marsh's test as to render it difficult to distinguish between them. When antimony is used in Marsh's test, however, the hydrogen flame has a tint which an expert can easily distinguish from arsenic. The spot produced by placing a clean piece of porcelain into the flame (which is none other than separated metallic antimony) is darker than the similar arsenic spot, and possesses less metallic luster. Moreover, it is insoluble in Labarraque's solution, while the arsenic spot dissolves readily in this reagent.

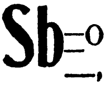
Three oxides of antimony are known, the antimonous oxide, Sb_2O_3, antimonic oxide, Sb_2O_5, and the third oxide, Sb_2O_4.

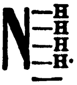
Sb_2O_4 can be considered as Sb_2O_3 plus Sb_2O_5, which would give us Sb_4O_8 or $2Sb_2O_4$. Besides, it can be regarded as antimonyl antimonate $(SbO)SbO_3$, to understand which the acid forms of antimony must be explained.

Already we have seen that nitrogen with valences III and V gives two oxides, N_2O_3 (nitrous) and N_2O_5 (nitric). Just so are the oxides of antimony, Sb_2O_3 and Sb_2O_5.

The nitrogen oxides, as shown on p. 392, yield, when added to water, nitrous and nitric acids respectively.

Exactly so Sb_2O_3 yields antimonous acid ($HSbO_2$) and Sb_2O_5 gives antimonic acid ($HSbO_3$). Antimonic acid will give salts, such as potassium antimonate ($KSbO_3$), and in Sb_2O_4 we have antimonyl antimonate—$(SbO)SbO_3$, antimonyl being a radical of valence I $(SbO)^{I}$, graphically


$\mathrm{Sb}\begin{smallmatrix}=\mathrm{O}\\ -\end{smallmatrix}$, just as ammonium is a radical with valence I $(NH_4)^{I}$, graphically


$\mathrm{N}\begin{smallmatrix}-\mathrm{H}\\ -\mathrm{H}\\ -\mathrm{H}\\ -\mathrm{H}\\ -\end{smallmatrix}$.

The "antimonyl," just spoken of, is found in the one official salt of antimony—tartar emetic.

The only preparations of antimony recognized in the present Pharmacopœia are:

Antimony and potassium tartrate. At least 99 per cent absolute $2K(SbO)C_4H_4O_6 + \frac{1}{2}H_2O$.

Compound mixture of glycyrrhiza, containing 240 mg. antimony and potassium tartrate to the liter.

ANTIMONII ET POTASSII TARTRAS—Antimony and Potassium Tartrate

(Antim. et Pot. Tart.—Antimonyl Potassium Tartrate, Tartrated Antimony, Tartar Emetic)

$K(SbO)C_4H_4O_6.\frac{1}{2}H_2O$. Molecular weight, 333.90

Antimony and Potassium Tartrate contains not less than 99 per cent $KOOC.CHOH.CHOH.COO(SbO).\frac{1}{2}H_2O$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless, rhombic crystals or white, granular powder; sweet, afterward disagreeable metallic taste; soluble in about 12 parts of water and about 12 parts of glycerin; insoluble in alcohol. For details, see U.S.P., p. 57.

For *tests for identity*, for *impurities* (iron, arsenic) and for *assay*, see U.S.P., p. 57.

Remarks.—This official, commonly called *tartar emetic*, is antimonyl and potassium tartrate, since the radical $(SbO)^1$ enters the compound rather than the element itself. Tartaric acid has the power of easily forming double salts. (See p. 400.) Rochelle salt was one of these double salts, and "tartar emetic" differs from Rochelle salt only in the substitution of antimonyl (SbO) for sodium:

$KNaC_4H_4O_6$ (Rochelle salt). $K(SbO)C_4H_4O_6$ (tartar emetic).

It is made by boiling the antimony oxide with potassium bitratrate and water for an hour. When so treated, the hydrogen of the potassium bitartrate is eventually replaced by the antimonyl group furnished by the antimony oxide.

Antimony and potassium tartrate, as its synonym would indicate, is used as an emetic, in large doses, while in small doses it acts as an alterative and diaphoretic and expectorant. It was formerly largely used as an emetic, but its action was so violent that it has largely fallen into disuse. If given in an overdose, the antidote is tannin.

Dose.—3 mg. (1/20 grain).

Tartar emetic is a constituent of *compound mixture of opium and glycyrrhiza* (p. 279).

Antimonii Oxidum (U.S.P. 1890; N.F. V), or *Antimony Oxide*, shows antimony with the valence III, it being the "ous" oxide, Sb_2O_3. It was the main ingredient of the *antimonial powder* (U.S.P. 1890).

The manufacture of this oxide is rather intricate. Antimony sulfide is first dissolved in hydrochloric acid, whereby soluble antimony chloride, *butter of antimony*, is produced:

$$Sb_2S_3 + 6HCl = 2SbCl_3 + 3H_2S.$$

The filtered solution is then poured into a large quantity of water, with the production of an insoluble oxychloride, shown by the following equation:

$$12SbCl_3 + 15H_2O = 2SbCl_3.5Sb_2O_3 + 30HCl.$$

This insoluble oxychloride (*powder of Algaroth*) is then treated with ammonia water, which converts it into the pure oxide, as is shown in the following equation:

$$2SbCl_3.5Sb_2O_3 + 6NH_4OH = 6Sb_2O_3 + 6NH_4Cl + 3H_2O.$$

This oxide is washed to free it from ammonium chloride and then dried.

The product is a white powder, insoluble in water and is used as an alterative in 1-grain doses.

Antimonial Powder (U.S.P. 1890; N.F. V), or *James' Powder*, is a galenic made by triturating 33 Gm. of the oxide with 67 Gm. of calcium phosphate.

Antimony Sulfide has been touched upon on p. 585. When hydrogen sulfide is passed through antimony solutions we get a precipitate that is sometimes red but usually orange in color. The red sulfide is Sb_2S_3; the orange sulfide has been considered as Sb_2S_5 but at present this is a subject of controversy, some investigators claiming that the orange sulfide is Sb_2S_4 containing varying quantities of free sulfur. Native antimony sulfide, on the other hand, is a black ore.

In U.S.P. 1890, three forms of antimony sulfide were official.

Antimonii Sulfidum (U.S.P. 1890), or *Antimony Sulfide*, is too crude for internal use, containing, as it does, a large quantity of arsenic. It is used quite largely in veterinary practice as an alterative under the name of *black antimony*, and should never be dispensed for human consumption. In many sections so-called "black antimony" used in veterinary practice consists largely of powdered coal.

Antimonii Sulfidum Purificatum (U.S.P. 1890) represented crude antimony sulfide, purified by washing with ammonia, the theory of this washing being that arsenic sulfide is soluble in ammonia water. However, antimony sulfide itself is somewhat soluble in ammonia water, and therefore the process is wasteful. Equally good results would be obtained, as far as freeing the sulfide from arsenic is concerned, by washing with a mixture of ammonia water and ammonium carbonate, in which solvent antimony sulfide is scarcely soluble.

The purified sulfide of antimony is used as an alterative in doses of 1 grain.

Antimonii Sulfuratum (U.S.P. 1890; N.F. IV), or *Kermes Mineral*, is made by boiling antimony sulfide with soda and precipitating the alkaline solution with sulfuric acid.

The equations occurring in this process are as follows:

$$(a)\ Sb_2S_3 + 6NaOH = Na_3SbO_3 + Na_3SbS_3 + 3H_2O.$$

$$(b)\ 2Na_3SbO_3 + 3H_2SO_4 = 3Na_2SO_4 + Sb_2O_3 + 3H_2O.$$

$$(c)\ 2Na_3SbS_3 + 3H_2SO_4 = 3Na_2SO_4 + Sb_2S_3 + 3H_2S.$$

Sulfurated antimony is an alterative and diaphoretic. It is much esteemed by French physicians, who find it a valuable constituent for cough mixtures, a favorite recipe for this purpose being 1 grain of sulfurated antimony in 1 ounce of syrup of wild cherry, a teaspoonful being given as a dose.

Compound Pills of Antimony (N.F. IV), or *Plummer's Pills*, consist of sulfurated antimony, powdered guaiac, and calomel. They are used in secondary syphilis, 1 or 2 pills being the dose.

Another unofficial antimony compound worth passing mention is *pyroantimonic acid*, $H_4Sb_2O_7$. This compound, as it will be seen, has the formula analogous to that of pyrophosphoric acid, already discussed on p. 496. Its potassium salt is being used for the detection of sodium, sodium pyroantimoniate being practically the only insoluble sodium compound.

TIN

Symbol, Sn. Atomic weight, 118.7

While this element yields no official compounds, it is of sufficient importance to justify passing notice.

The source of tin is the oxide, SnO_2, which is commonly called *tin stone*, and mined very largely in Cornwall, England, Malacca, and Bolivia. The little produced in the United States is mined in South Dakota.

Tin has been used for many centuries, Pliny's *kassiteros* (or plumbum candidum), which he says came from the Cassiterides in the Atlantic. Whether the Cassiterides was Britain or islands off Spain is a matter of controversy.

The metallurgy of tin, like that of so many other metals, is accomplished by heating together coal and the oxide, freed from sulfur and arsenic by roasting, the reaction being as follows:

$$SnO_2 + C = Sn + CO_2.$$

Tin is a brilliant white metal, very malleable, and thus can be made out into very thin sheets, which are much used by pharmacists under the name of *tin foil.* The so-called *tin plate* consists of sheets of iron coated with tin, either by dipping the iron into the molten metal or by rolling the tin upon the iron plate.

Tin compounds are tested as follows: potassium hydroxide produces a white precipitate of tin hydroxide; ammonium sulfide produces a black precipitate when a stannous salt is under treatment (stannous sulfide); a yellow precipitate of stannic sulfide, if the tin compound is of the higher valence. The special test for stannous tin is the fact that if a solution of mercuric chloride is mixed with a solution of stannous salt, the mercuric salt is reduced to metallic mercury, with a corresponding separation of the metal as a gray precipitate.

Two oxides of tin are known, stannous oxide, SnO, and the stannic oxide, SnO_2. In these, as in the other tin compounds, the stannous form of tin exhibits the valence II, while the stannic form shows valence IV.

No compounds of tin are official. The following, however, are of passing interest in pharmaceutic chemistry.

Stannous chloride, $SnCl_2$, is made by treating the metal with hydrochloric acid, and is used in analytic work as a reducing agent, as shown in the mercury test for stannous compounds that has just been given.

Stannic chloride, $SnCl_4$, was first made by Libavius (1605) by distilling tin with mercuric chloride. When water free, it is a colorless, fuming liquid, which was formerly known as *spiritus fumans Libavii.*

Tin, like zinc and aluminum, stands midway between the positive and negative elements, and while generally acting as a metal in its compounds, it forms, with alkalis, salts of stannic acid, H_2SnO_3. The sodium salt, Na_2SnO_3, is used largely in calico printing under the name of "*tin salt.*"

French clinicians report that various tin compounds and especially *colloidal tin* are of value in the treatment of staphylococcic infections, such as boils. Some proprietary preparations containing tin salts have been offered for that purpose.

GOLD

Symbol, Au. Atomic weight, approximately 197

Gold is usually found in the native, uncombined form, being associated with either sand or quartz. It is beyond the limits of this work to go into extended consideration of the production of gold, and therefore suffice it to say that it is found in certain sections of the world, such as, for instance, California, Alaska, Canada, Australia, and South Africa.

The mining of gold is accomplished in several ways, according to the condition in which the metal is found. When found associated with sand, it is usually extracted from the beds of rivers. In this case the gold is separated from the sand by the process of washing, which can be compared to levigation. (See p. 138.) If done on a small scale, the mixture is placed in a pan, and washed rapidly with water, whereby the sand is washed out, leaving the heavier gold in the bottom of the pan. The washing is performed on a large scale by the process of "placer-washing," which consists of putting the gold-bearing sand into the upper one of a series of long troughs, each trough being slightly lower than its predecessor.

Into the top trough is run a good stream of water (usually from an adjacent mountain torrent), which, passing continuously through, gradually throws out all the sand, and, at the same time, a large quantity of the gold. The mixture of sand and gold passes to a second trough, where a considerable quantity of the gold separates out, while all the sand is washed out into the third trough. And thus the process goes on until all the sand has been removed, while practically all the gold remains in the troughs.

The crude gold is purified by the amalgamation process—that is, it is treated with mercury—and the amalgam then submitted to distillation when the mercury passes over, leaving the gold in the still.

When gold is found in quartz, the gold is extracted by either of two methods.

In the *chlorination process* the ore is roasted to remove sulfur and arsenic, the residue is mixed with water and treated with chlorine. Gold is separated from the resulting gold chloride solution by precipitation with ferrous sulfate.

In the *cyanide process* the finely ground ore is percolated with a dilute solution of potassium cyanide, which dissolves the gold as a double cyanide. The metal is separated from the percolate by electrolysis.

Gold is one of the most ancient of metals, ornaments of the metal being found in the Egyptian tombs. The Latin word for gold, *aurum*, is of classic origin, being derived from the Hebrew word *zohov*, which meant the color of fire. It is of interest to note that in many of the ancient languages the word distinguishing gold is the same word used to signify yellow.

Gold is a soft yellow metal, having the specific gravity about 19. It is the most malleable of all metals, capable of being beaten into sheets (leaves) so thin that 280,000 of them are required to measure an inch. When beaten out so thinly, the sheets are translucent, and the light transmitted through them is of a greenish color. Gold is also a very ductile metal, although it is not capable of being drawn into wire as thin as is platinum. It is not soluble in nitric acid nor in hydrochloric acid, but it does dissolve in a mixture of the two—aqua regia (see p. 455)—which is supposed to act on the metal, not by reason of the composition of either of the constituents, but because of the free chlorine and nitrosyl chloride contained in the nitrohydrochloric acid. Because of the softness of the pure metal, gold is always employed in the form of an alloy.

According to Ridgeway, the total production of gold from 1493 to 1927 was 1,003,500,000 ounces; of which 516,273,000 was mined from 1900 to 1927. Of total production (1493–1927) 28 per cent was mined in North America. In 1931, 53 per cent of all the gold mined came from South Africa.

The gold coins of America consist of 90 per cent of gold and 10 per cent of copper, while the gold used in making jewelry contains a still larger quantity of copper. The rating of the gold content of jewelry gold is not by percentage, but by a clumsy commercial standard called *karats*. Pure gold is said to be 24 karats. Hence when we speak of 14-karat gold we mean that it is $^{14}\!/_{24}$ gold. *White gold* is an alloy of gold with such metals as platinum, palladium, nickel or zinc. The cheaper types contain the two metals last mentioned. *Rolled gold* is a baser metal coated with gold either by "sweating" or by soldering.

The *tests* for gold are as follows: hydrogen sulfide gives the black precipitate of gold sulfide. When a fresh solution of ferrous sulfate is added to a solution of gold salt, gold separates out, and when gold salts are treated with tin chloride in the presence of a ferric salt, a beautiful purple color is produced. This purple substance, which is a mixture of colloidal gold and colloidal stannic acid, was formerly used as a pigment under the name of *purple of Cassius.*

Gold usually exhibits the valence III, although monovalent gold is known in such compounds as AuCl and Au_2O.

No gold salt is recognized by U.S.P. X, although U.S.P. IX and earlier Pharmacopœias recognized:

Auri et Sodii Chloridum (U.S.P. IX) which was a mixture of equal parts of anhydrous gold chloride, $AuCl_3$, and anhydrous sodium chloride, NaCl.

Gold chloride is quite hygroscopic, and to lessen this disagreeable quality as much as possible the former Pharmacopœia directed it combined with an equal weight of "decrepitated" sodium chloride. Decrepitated salt means that from which the interstitial water has been driven by heat. Salt, when heated, crackles, because the interstitial water forms steam which explodes with sufficient force to break the crystals.

Gold chloride is made by dissolving gold in aqua regia. The filtered solution is then evaporated, when there crystallizes chlorauric acid, $HAuCl_4.4H_2O$.

If this be mixed with sodium chloride, true gold and sodium chloride, $AuCl_3.NaCl.2H_2O$, results. This is not the formerly official body, which, as above stated, is made by triturating dried gold chloride with an equal quantity of dried salt.

Gold chloride is best made by treating gold with chlorine, since the product obtained by evaporation of an aqua regia solution is apt to contain aurous chloride, AuCl.

Gold and sodium chloride is used as an alterative. Gold chloride and other compounds have been much vaunted as remedies for the drink habit. That the so-called "gold cure" is efficient cannot be denied, but whether due to the gold or to the other stimulants employed is a matter still open for discussion. *Dose.*—5 mg. ($^1\!/_{12}$ grain).

Acidum Bromauricum (N.F. V) or *bromauric acid*, $HAuBr_4.5H_2O$, is a definite compound of gold bromide and hydrobromic acid. It contains 32 per cent metallic gold. It is used as an alterative in $^1\!/_{10}$-grain doses.

Liquor Auri et Arseni Bromidi (N.F. V) is made by preparing arsenic bromide (heating together, arsenic trioxide, bromine and water) and then adding to the pure bromide solution, bromauric acid. It represents one fourth of 1 per cent of As_2O_3 and about one third of 1 per cent of bromauric acid.

Colloidal Gold.—Of recent years much research has been devoted to colloidal gold. The ancient physicians discussed "aurum potabile" which was apparently a crude form of colloidal gold. The "purple of Cassius" test just described is another manifestation of colloidal gold.

Pauli prepares gold "sols" by the electrolytic treatment of ordinary gold salts. He finds that the colloidal gold found in these "sols" consists of a metal nucleus to which is attached aurates or more complex acids of gold.

Nicol and others prepare the "sol" by treating a solution of a gold salt with hydrogen peroxide in the presence of alcohol. These gold "sols" are used in treatment of tuberculosis and of epilepsy.

Gold Therapy.—For the past fifteen years considerable attention has been paid in the medical literature to the treatment of tuberculosis by the use of certain compounds of gold: notably the double thiosulfate of gold and sodium, which was introduced by Moellgaard under the name *sanocrysin.* Among other gold preparations used similarly are *aurocantan, aurolin, krysolgan, solganol,* and *lopion.*

PLATINUM

Symbol, Pt. Atomic weight, approximately 195

Platinum occurs native, and is found in Columbia, Brazil, and chiefly in the Ural Mountains. The metal thus obtained is always contaminated with palladium, iridium, osmium, ruthenium, and the separation of these precious metals is a matter of considerable difficulty.

Platinum was first brought to the attention of the world by de Ulloa, in 1748, who, in his descriptions of his explorations of Mexico, referred to the metal there discovered. The word *platina* (little silver) was first applied to the metal by Scheffer in 1752.

Platinum is the most ductile of all metals, it having been drawn into wire so thin that a microscope is required to see the strand. It is one of the most difficult of the metals to be fused, and for this reason it is of great value in the making of crucibles or similar vessels to be used for high heat. (See p. 99.) It must be noted, however, that platinum utensils are by no means unaffected by any substance, experience having shown that the metal forms a fusible alloy with lead and a fusible phosphide with phosphorus; that also alkaline hydrates, sulfides, hypophosphites, and cyanides attack the platinum, eventually eating through the same; so none of these substances should be heated in platinum dishes.

Spongy platinum is an interesting form of the metal. It is made by heating platinoammonium chloride (see below) until all the ammonia and chlorine have been driven off, leaving a spongy lump of platinum which possesses remarkable absorptive capacity for oxygen, it being stated that one volume will absorb 250 volumes of that gas. The oxygen thus absorbed is in condition readily to combine with other substances, notably hydrogen, and this principle was made use of in the so-called "Doebereiner's lamp," which was largely used before the introduction of matches. This lamp consists of an ordinary hydrogen generator, with a piece of spongy platinum placed near the nozzle, from which the hydrogen gas would be emitted. As soon as a stream of hydrogen is played on the spongy platinum, a chemical union between oxygen (from the air) and hydrogen takes place, with a heat sufficiently intense to cause the ignition of the hydrogen, and thus producing flame.

Spongy platinum is the catalyst used in the contact process for making sulfuric acid (see p. 449).

Another interesting point connected with platinum is the fact that at red heat a sheet of platinum permits hydrogen to pass through it, no other gas being thus given transit. This phenomenon has been made use of for the removal of hydrogen from a mixture of gases.

The *tests* for platinum are as follows: Hydrogen sulfide produces a brown sulfide, and potassium chloride added to a solution of platinic chloride will produce the characteristic yellow crystals. These crystals have already been discussed under Potassium. A similar precipitate of platinic ammonium chloride is produced when ammonium chloride is also treated with platinic chloride.

No salts of platinum are official, but *platinic chloride,* $PtCl_4$, is mentioned in the appendix to the Pharmacopœia as a constituent of the test solution used for detection of potassium.

The platinum market during the past twenty years has shown remarkable fluctuations. Prior to the World War practically all of the metal was mined in Russia where, in 1913, 250,000 ounces were produced. With the chaotic conditions obtaining in that country since 1914, the Russian production slumped to almost zero during 1914-1920 and in 1927 had slowly climbed to 100,000 ounces. In the meanwhile, other countries began to market platinum as the following figures show: Colombia (1926), 40,000 ounces; South Africa (1928), 23,600 ounces; and Canada (1930), 30,000 ounces. During these days of platinum shortage a number of substitutes for the metal were devised, for use in analytical chemistry. Among these may be cited *palau, pallas, alargan, platargan, platnik,* and *konel.* For details the reader is referred to the bibliography found at the end of this chapter.

BIBLIOGRAPHY

Arsenic.—(History) Maurantonio, L'arsenico, Milan, 1912; Brunton, St. Louis Congress of Arts and Sciences, 6, 1904, 177; Heisch, Ph. Jl., [2], 1, 1860, 556; Roscoe, Mem. Lit. Phil. Soc. Manchester, [3], 1, 1862, 208; Hackh, A.J.P., 90, 1918, 492;

Schwartze, J. Pharmacol. Exp. Therap., 20, 1923, 181. (Sources) Anon., Pract. Dr., 29, 1911, 25; Bailey, Pharm. Era, 61, 1925, 655. (Solubility) Trease, C.A., 22, 1928, 3954; Bryant, Ph. Jl., 130, 1933, 175. (Tests) Marsh, A.J.P., 8, 1837, 307; Lockemann, Ch. Zt., 36, 1912, 1465; Fleitmann, A., 77, 1851, 126; Gutzeit, Schweigger's Jl., 53, 1828, 377; Reinsch and Adouard, A.J.P., 15, 1842, 269; Bettendorff, Ch. News, 20, 1869, 189; Vanino and Hartwagner, C.A., 9, 1915, 38; Bornemann, Jl. Soc. Ch. Ind., 41, 1922, 946A; Chapman, *ibid.*, 42, 1923, 124; Willcox, Jl. Soc. Ch. Ind., 43, 1924, 1172; King, *ibid.*, 46, 1927, 556; Leffman, Jl. Frank. Inst., 207, 1929, 430. (Toxicity) Fabian, A.J.P., 33, 1861, 314; Sanger, A.Ph.A., 42, 1894, 1013; Taylor, A.J.P., 30, 1858, 275; Schwartze and Munch, A.J.P., 98, 1926, 604; Scheringa, C.A., 22, 1928, 3470; Dyson, Ph. Jl., 122, 1929, 72, 146, 199 and 225. (Medical uses) Smith, Jl. A.Ph.A., 11, 1922, 423. (Technical uses) Knapp, Jl. Soc. Ch. Ind., 44, 1925, 607. (Colloidal arsenic) Gutbier and Kräutle, C.A., 11, 1917, 3140.

Fowler's Solution.—(History) Richardson, Dr. Circ., 9, 1865, 17; Langenhan, Jl. A.Ph.A., 8, 1919, 189; Cooper, Spatula, 27, 1920, 7; Anon., Pract. Dr., 41, June, 1923, 15; Raubenheimer, Jl. A.Ph.A., 18, 1929, 270. (Composition) Bullock, Ph. Jl., 10, 1850, 358; Lyons, A.Ph.A., 57, 1909, 907; Rhemthaler, Schweiz. Wsch., 50, 1912, 569. (Stability) Danckwortt, Jl. Soc. Ch. Ind., 44, 1925, 188B; Trease, C.A., 23, 1929, 241.

Arsenous Acid.—(Composition) Bloxham, Jl. prakt. Ch., [1], 87, 1862, 114; Walden, Zt. phys. Ch., 2, 1888, 50.

Sodium Arsenate.—(Manufacture) Anon., A.Ph.A., 11, 1863, 126. (Toxicity) Bridel, Jl. Ph. Ch., 28, 1923, 395.

Arsenous Iodide.—(Manufacture) Plisson, Jl. de ph., 14, 1828, 46 and 592; Berthelot, Comp. rend., 86, 1878, 862; Nickles, Jl. de ph. et ch., 36, 1859, 161; Fish, A.J.P., 13, 1841, 97.

Donovan's Solution.—(History) Donovan, Ph. Jl., 2, 1842, 469 and 546. (Composition) Langenhan, Jl. A.Ph.A., 14, 1925, 579. (Deterioration and preservation) "Thuja,' A.J.P., 31, 1859, 410; Huskisson, Ph. Jl., [2], 11, 1869, 285; Cocking, Quart. Jl. Ph., 2, 1929, 409; Schulze, Jl. A.Ph.A., 15, 1926, 965; Acton, A.J.P., 102, 1930, 159; Husa, Jl. A.Ph.A., 19, 1930, 328, 1228 and 1287; 21, 1932, 211; Dr. Circ., 77, Feb., 1933, 17.

Antimony.—(History) Arny, Am. Dr., 39, 1901, 3; Schelenz, Dr. Circ., 54, 1910, 262; Anon., Nat. Dr., 44, 1914, 155; Babcock, Am. Dr., 17, 1888, 202; Lloyd, Dr. Circ., 52, 1908, 454; Ekert, Sch. Wsch. Ch. Ph., 51, 1913, 193 and 209; Redwood, Ph. Jl., 18, 1858, 14; Hackh, A.J.P., 90, 1918, 491; Hommel, Z. angew. Ch., 32, I, 1919, 73; Hyman, Jl. Soc. Ch. Ind., 43, 1924, 1006; Chapman, *ibid.*, 43, 1924, 1058; Fritz, Zt. angew. Ch., 38, 1925, 325; Pope, Ph. Jl., 130, 1933, 142. (Sources) Halse, Jl. Soc. Ch. Ind., 44, 1925, 485; Pascoe, *ibid.*, 49, 1930, 52; Anon., *ibid.*, 51, 1932, 617.

Tartar Emetic.—(History) Babcock, Am. Dr., 17, 1888, 203. (History and manufacture) Chevallier, A.J.P., 1, 1829, 287. (Constitution) Clarke and Evans, B., 16, 1883, 2386; Linnell and Tickle, C.A., 22, 1928, 4717; Satullo, C.A., 23, 1929, 1687; Wark, C.A., 26, 1932, 666; Reihlen and Hezel, C.A., 25, 1931, 4852. (Properties) Dunsten and Boole, Ph. Jl., [3], 191, 1888, 397.

Butter of Antimony.—(History and manufacture) Babcock, Am. Dr., 17, 1888, 203; Chevalier, A.J.P., 1, 1829, 287.

Powder of Algaroth.—Babcock, Am. Dr., 17, 1888, 204.

James' Powder.—(History) Unzicker, Dr. Circ., 9, 1865, 107; Babcock, Am. Dr., 17, 1888, 204.

Antimony Sulfides.—Kirchhoff, C.A., 15, 1921, 1469; Twiss, C.A., 16, 1922, 2620; Milbauer, Jl. Soc. Ch. Ind., 50, 1931, 552B; Hansen, C.A., 26, 1932, 5389.

Black Antimony.—McGill, C.A., 6, 1912, 271.

Kermes Mineral.—(History) Liance, A.J.P., 20, 1848, 233.

Tin.—(History) Hackh, A.J.P., 90, 1918, 491; Partington, Atkinson and others, Jl. Soc. Ch. Ind., 42, 1923, 671 and 696; Thornewell, Jl. Soc. Ch. Ind., 48, 1929, 633; Dyson, Ph. Jl., 126, 1931, 299 and 498. (Metallurgy) Hutchison and Wayte, C.A., 14, 1920, 921; Van Gelden, *ibid.*, 17, 1923, 1777; Anon., C.A., 10, 1916, 1135; Hollister, C.A., 10, 1916, 1625. (Sources and production) Anon., Jl. Frank. Inst., 200, 1925, 334; Edit., Jl. Soc. Ch. Ind., 48, 1929, 590; Anon., Jl. Ind. Eng. Ch., 23, 1931, 1113. (Medical uses) Podolsky, Pract. Dr., 49, Apr., 1931, 28.

Tin Plate.—Goldschmidt, Z. angew. Ch., 22, 1909, 1; Griffiths, Jl. Soc. Ch. Ind., 50, 1931, 431.

Gold.—(History) Anon., Keystone Weekly, 41, 1914, 71; Hackh, A.J.P., 90, 1918, 489; Dyson, Ph. Jl., 123, 1929, 249. (Extraction) Ellis, Eng. Min. Jl., 99, 1915, 805; Aitken, Ph. Jl., 94, 1915, 693; Butters and Clennell, Jl. Soc. Ch. Ind., 11, 1892, 916; Spearman, Jl. Soc. Ch. Ind., 44, 1925, 174T; Kendall and Hosking, *ibid.*, 44, 1925, 43B; Clark, C.A., 25, 1931, 1775; Stroup, A.J.P., 105, 1933, 76. (Production) Young, C.A., 24, 1930, 4490; Ridgeway, Science, 71, 1930, 208; Edit., Jl. Soc. Ch. Ind., 50, 1931, 806; Graton, C.A., 25, 1931, 1185; Hadfield, Jl. Soc. Ch. Ind., 51, 1932, 374; Anon., *ibid.*, 51, 1932, 300; Fleck, *ibid.*, 52, 1933, 57.

Gold Leaf.—Abegg and Auerbach, 2^2, 1908, 783; Pope, Jl. Soc. Ch. Ind., 44, 1925, 654; Griffith, A.J.P., 101, 1929, 157.

White Gold.—Nowack, C.A., 23, 1929, 3429 and 24, 1930, 5267; Thews, C.A., 26, 1932, 66; Anon., Jl. Frank. Inst., 214, 1932, 508.

Rolled Gold.—Smith, C.A., 24, 1930, 5265.

Purple of Cassius.—Gruenewald, Sprechsaal, 43, 1911, 419; Anon., A.J.P., 6, 1834, 85; Huber, Jl. Soc. Ch. Ind., 43, 1924, 292B; Levi and Fontana, C.A., 22, 1928, 338 and 1067; Dyson, Jl. Soc. Ch. Ind., 48, 1929, 938.

Colloidal Gold.—Paal, Jl. Soc. Ch. Ind., 21, 1902, 916; Darmstaedter, Jl. Soc. Ch. Ind., 43, 1924, 1207; Keulemans, Ph. Weekbl., 65, 1928, 647; Nicol, Jl. Soc. Ch. Ind., 47, 1928, 343T and 48, 1929, 100T; Iwase, C.A., 25, 1931, 1425; Pauli, C.A., 24, 1930, 2932; 26, 1932, 2102 and Jl. Ind. Eng. Ch., News Ed., 10, 1932, 162.

Gold Therapy.—De Witt, C.A., 11, 1917, 3333; Moellgaard, Ch. and Dr., 102, 1925, 889; Greenbaum, A.J.P., 98, 1926, 471; Dyson, C.A., 24, 1930, 2546; Mignot, C.A., 24, 1930, 3279.

Gold Chloride.—Petit, Jl. Soc. Ch. Ind., 44, 1925, 918B.

Gold and Sodium Chloride.—(Composition) Kruss, A., 238, 1887, 241. (Manufacture) Sothien, Arch. d. Pharm., 220, 1882, 202. (Uses) Bouhila, A.J.P., 64, 1892, 466.

Platinum.—(History) Gmelin-Kraut, 5^3, 1914, 3; Hackh, A.J.P., 90, 1918, 568; Howe and Holtz, U. S. Geol. Survey Bull., 694, 1919, 1–454; McDonald, Jl. Soc. Ch. Ind., 50, 1931, 1031; Meyer, Science, 75, 1932, 438. (Sources) Merz, Jl. Ind Eng. Ch., 10, 1918, 920; Hill, Pharm. Era, 51, 1918, 173; Thompson, A.J.P., 92, 1920, 114. (Production) Anon., A.J.P., 95, 1923, 928; Anon , Jl. Soc. Ch. Ind., 44, 1925, 135, 535 and 684; Anon., Jl. Ind. Eng. Ch., News Ed., 7, Mch. 20, 1929, 8; Cook, *ibid.*, 9, 1931, 191. (Extraction) Wollaston, A.J.P., 1, 1829, 70. (Properties) Sobolewskcy, Jl. de ph., 21, 1835, 181; Deville, Ph. Jl., [2], 1, 1860, 416 and 465; Ribaud and Mohr, C.A., 25, 1931, 1720; Roeser and co-workers, C.A., 25, 1931, 4751. (Uses) Anon., Pharm. Era, 52, 1919, 44. (Substitutes) Van der Marck, Pharm. Weekbl., 55, 1918, 149; Heath, Met. Ch. Eng., 1918; Anon., C.A., 11, 1917, 2627; Gawalowski, C.A., 19, 1925, 1969; Quadrat and Jiriste, Jl. Soc. Ch. Ind., 49, 1930, 62B; Anon., Jl. Frank. Inst., 213, 1932, 96.

CHAPTER XXXIII

CADMIUM, COPPER, AND BISMUTH

CADMIUM

Symbol, Cd. Atomic weight, 112.4

CADMIUM is a mineral which is usually found in combination with zinc; most calamines containing cadmium. The most important cadmium mineral is *greenockite*, which is chiefly cadmium sulfide.

The name is derived from the Greek word *kadmia*, which was the ancient name for calamine. The element was isolated from this ore by Strohmeier in 1817.

Cadmium is a white metal, like tin, and like it crackles when bent; it has a higher specific gravity, however, and is more tenacious.

The *tests* for cadmium are the yellow sulfide, produced by treating solutions of the salts with hydrogen sulfide or with ammonium sulfide, and the white hydroxide, precipitated when the solution of the salt is treated with potassium hydroxide or ammonium hydroxide. This hydroxide is insoluble in an excess of potassa, but soluble in an excess of ammonia. Sodium carbonate precipitates cadmium salts in the form of white cadmium carbonate, which is insoluble in an excess of the reagent.

Cadmium usually exhibits the valence II, as shown in the oxide, CdO. No salts of cadmium are official. The metal is sometimes used in amalgam (see p. 610) fillings used in dentistry.

Of late years the commercial production of cadmium has increased to about 2000 tons per annum and the metal is now used quite largely for electrocoating iron to prevent rust and for preparing electric batteries. Cooper and his coworkers find cadmium compounds are distinctly germicidal; being more potent than lead compounds and less so than mercury compounds.

COPPER

Symbol, Cu. Atomic weight, approximately 63

This important metal is found in nature as metallic copper; also is found in the ore *copper glance*, Cu_2S; also as cuprous oxide, while native copper carbonate forms a beautiful green mineral, *malachite.*

Copper has been known from the most ancient times, its name, cuprum, coming from *cyprum*, the isle of Cyprus, where the ores were first mined. The metallurgy of the copper ores depends upon the character of the ore. If the ore is chiefly copper oxide, the separation is easily effected by heating ore with carbon, as expressed in the following equation:

$$Cu_2O + C = Cu_2 + CO.$$

Sulfides, on the other hand, are first roasted with sand and some substance which will act as a flux. This action partially converts the ore into copper oxide. By heating this mixture, sulfur dioxide is liberated and copper remains, as expressed by the following equation:

$$CuS + 2CuO = 3Cu + SO_2.$$

Chemically pure copper is prepared by the electrolysis of copper sulfate.

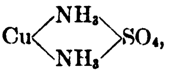
Reference should be made to the now largely used metallurgical process of *flotation*, a method of separating the metalliferous particles of an ore from the useless portion, such as quartz and other silicates. The process is based upon the physical fact that when the ore is finely powdered the metalliferous particles are wetted by certainly oily liquids but not by water whereas the quartz and other silicates are wetted by water and not by oil.

In actual practice, the oily fluid plus the activating reagent plus water are passed through troughs with constant agitation when a froth is formed, upon which float the metalliferous particles while the quartz particles become wetted by the water and sink to the bottom of the trough. The froth and its metalliferous particles are automatically separated from the water layer; the oily portion is separated from the metalliferous particles by centrifuging and the concentrate, the oxide or the sulfide of the metal, is then treated by roasting with or without carbon as described above. The oily liquids used in modern flotation are petroleum and pine oils. The activating reagents include frothers such as creosotes and organic reactants such as ethyl and other xanthates. For further details the reader is referred to the articles listed in the bibliography at the end of this chapter.

Copper is a brilliant red metal, ductile and malleable. When chemically pure, it is an admirable conductor of electricity, and its use for this purpose is so extensive that the supply is scarcely equal to the demand. The metal is insoluble in either diluted hydrochloric acid or diluted sulfuric acid, except in presence of air, but it does dissolve in concentrated sulfuric acid with the formation of copper sulfate.

An important use of copper is in the formation of the well-known series of alloys. Thus *brass* is made by the fusion of 3 parts of copper and 1 part of zinc. *Bronze* represents the mixture of copper, tin, zinc, and lead. *Japanese bronze* contains gold and silver, in addition to the metals above given. *Phosphor bronze* consists of 90 per cent of copper, 9 per cent of tin, and 1 per cent of phosphorus. This is a remarkably tough and durable alloy, and is, therefore, of great value in making metallic bearings. *Manganese bronze* contains about 56 per cent of copper, 42 per cent of zinc, not more than 0.3 per cent of manganese and small amounts of tin, aluminum and lead. *Monel metal* consists of nickel and copper with small amounts of manganese, iron, and silicon. Copper coins usually consist of 95 per cent of copper, 4 per cent of tin, and 1 per cent of zinc.

The *tests* for copper are: the black sulfide produced by treatment with hydrogen sulfide or ammonium sulfide; the brown-red copper ferrocyanide formed when a solution of a copper salt is treated with potassium ferrocyanide and the green color a copper salt transmits to a colorless flame. More characteristic, however, is the reaction of copper salts with ammonia. When such solutions are treated with concentrated ammonia water, the blue cupric oxide is precipitated. If, on the other hand, the copper solution is treated with an excess of ammonia, the blue precipitate redissolves, with the formation of an azure-blue solution. This solution contains ammoniated copper sulfate, having the following formula,



$$Cu\begin{matrix}\diagup NH_3 \diagdown \\ \diagdown NH_3 \diagup\end{matrix}SO_4,$$

and is quite characteristic. It must be borne in mind, however, that nickel salts, when treated with ammonia, give a similar azure-blue solution. If metallic zinc or iron is brought in contact with a copper salt, an electrolytic action sets in, with the deposition of metallic copper on the other metal. This can be demonstrated by dipping into a copper solution a steel spatula, which, on removal, will be found plated with copper. As mentioned on p. 299, this test is a simple way for detecting the presence of copper in vegetable extracts.

Three oxides of copper are known—Cu_2O, CuO, and CuO_2.

Cu_2O (cuprous oxide) is a brick-red precipitate obtained by treating copper sulfate with an alkali in the presence of a reducing agent. It is best demonstrated in testing substances containing glucose (example, diabetic urine) with Fehling's solution. (See p. 1028.)

Cupric oxide, CuO, occurs in the form of black granules or powder; while copper superoxide, CuO_2, is a yellowish-brown powder. The existence of Rose's suboxide, Cu_4O, is now doubted.

Cuprous and cupric hydroxides are also known.

But one salt of copper is official—

CUPRI SULFAS—Cupric Sulfate
(Cupr. Sulf.—Copper Sulfate)

$CuSO_4.5H_2O$. Molecular weight, 249.71

Cupric Sulfate contains not less than 63 per cent and not more than 66.8 per cent of $CuSO_4$, corresponding to not less than 98.5 per cent of the hydrated salt ($CuSO_4.5H_2O$).

Storage.—Preserve in air-tight containers.

Summarized Description.

Deep blue triclinic, efflorescent crystals or blue, granular powder; nauseous, metallic taste, soluble in about 3 parts of water, in about 400 parts of alcohol and in about 3.1 parts of glycerin; on heating, first exsiccates and finally dissociates into oxygen, sulfur dioxide and cupric oxide. For details, see U.S.P., p. 133.

For *tests for identity*, for *impurities* (other metals) and for *assay*, see U.S.P., p. 134.

Remarks.—This substance is known as *blue vitriol*, as already mentioned on p. 446. It is made by treating copper with sulfuric acid, and according as the acid is diluted or concentrated the reaction differs. When copper is treated with diluted sulfuric acid, the equation runs as follows:

$$Cu + H_2SO_4 + \underset{\left(\substack{\text{From the}\\ \text{air}}\right)}{O} = CuSO_4 + H_2O.$$

while if the metal is treated with hot concentrated sulfuric acid, the equation is as given below:

$$Cu + 2H_2SO_4 = CuSO_4 + SO_2 + 2H_2O.$$

It is interesting to note that in neither case is hydrogen produced, as frequently occurs when a metal is treated with sulfuric acid.

Both Cundall and Rogers believe that the reaction is more complex than is expressed in the simple equation just given.

Large amounts of crude blue-stone are made by roasting various copper ores and treating the residue with sulfuric acid.

Of the tests given above, its efflorescence and exsiccation are matters of interest; the fifth molecule of water of crystallization, held until the salt is heated to 200° C., being an illustration of water of constitution (p. 518).

Copper sulfate, when given in small doses, acts as an astringent or tonic. If given in large doses, it acts as an emetic, and was formerly considerably used for this purpose. Its action, however, is too irritating to recommend its use in these days. Applied externally in the form of a moistened crystal it is caustic, while a dilute solution is used as an astringent injection in gonorrhea.

Dose.—Emetic, 300 mg. (5 grains).

Cupric Acetate, which was recognized in the Pharmacopœia of 1880, is called *verdigris*, and was formerly in considerable use as an application for ringworms and other skin troubles.

Paris Green, or *Copper Aceto-arsenite*, is made by treating copper sulfate with sodium acetate and sodium arsenite. It therefore resembles Scheele's green. (See p. 580.)

BISMUTH

Symbol, Bi. Atomic weight, approximately 209

Bismuth is found in nature; it also occurs as sulfide in the ore, *bismuth glance*. The word bismuth is derived from the German *Wismuth*, the origin of this term being supposedly from the two German words *Wiese matte*, beautiful meadow. This, however, has been pronounced by Husemann to be merely a pleasant fable, his researches proving that the first mention of the metal in the Bergbuchlein of 1518 was under the name of *Wyssmut*. Hackh states that the name is derived from the Arabic "wiss majat," meaning "easy melting."

The extraction of the metal from the sulfide is accomplished by roasting in a reverberatory furnace, thus forming bismuth oxide, as shown in the following equation:

$$Bi_2S_3 + O_9 = Bi_2O_3 + 3SO_2.$$

On heating bismuth oxide with coal, carbon dioxide is liberated, and metallic bismuth remains,

$$2Bi_2O_3 + C_3 = 2Bi_2 + 3CO_2.$$

Bismuth is a crystalline, brittle, pulverizable, brilliant metal of silvery color, with, however, a slight reddish tint. In many of its qualities it resembles antimony.

The chief use of the metal is for the formation of fusible alloys, it possessing the characteristic property of blending with certain metals to form an alloy, melting at a temperature much below the melting point of any of the metals when heated alone. Thus, 2 parts of bismuth, 1 part of lead, and 1 part of tin, the melting point of the metals being respectively 271° C., 327° C., and 232° C., melts at 94° C. (Rose's fusible metal), while Wood's metal, consisting of 4 parts of bismuth, 1 part of cadmium, 1 part of tin, and 2 parts of lead, melts at 60.5° C. The chief use of such fusible metals is for automatic fire sprinklers, these consisting of water pipes passing along the ceiling of a room, punctured with holes which are plugged with the fusible metal. If a fire breaks out in the apartment, as soon as the temperature reaches 65° C., the metallic plugs melt and streams of water are thrown into the room. Pieces of these metals are also used as safety fuses in electric wiring.

Tests.—Bismuth, like so many metals of this group, gives a black sulfide when treated with hydrogen sulfide or ammonium sulfide. A more characteristic test is the fact that acid solutions of bismuth salts, when poured into water, produce a white precipitate of a "sub"-salt. Thus, bismuth nitrate solution, when poured into water, forms bismuth subnitrate, which precipitates out in the form of a white powder.

Three oxides of bismuth are known:

BiO or (Bi_2O_2), which is a black substance; B_2O_3, bismuthous oxide, a yellow powder; and Bi_2O_5, which is red in color.

The bismuthous oxide is the one ordinarily found.

The following compounds of bismuth are official:

Bismuth subcarbonate—approximately $(BiO)_2CO_3$—should yield at least 90 per cent absolute bismuth oxide.

Bismuth subgallate—approximately $BiC_7H_7O_7$—should yield from 52 to 57 per cent absolute bismuth oxide.

Bismuth subnitrate—approximately $BiONO_3$—should yield at least 79 per cent absolute bismuth oxide.

Bismuth subsalicylate—approximately $Bi_2O_3(C_7H_5O_3)_3$—should yield from 62 to 66 per cent absolute bismuth oxide.

Bismuth and potassium tartrate should yield from 71 to 75 per cent of absolute bismuth oxide.

Bismuth Hydroxide, $Bi(OH)_3$, is produced when an acid solution of bismuth nitrate is treated with a soluble hydroxide, preferably a diluted ammonia water. The magma thus produced, when mixed with water, has been popular under such names as *bismuth cream* or *bismuth milk.* Such a preparation is recognized by the National Formulary under the name:

Magma Bismuthi (U.S.P. IX; N.F. VI).—This is made by the following method. Dissolve 80 Gm. bismuth subnitrate in a mixture of equal volumes of nitric acid and water and mix this with a diluted nitric acid. Dilute 480 cc. of ammonia water with water, dissolve therein 10 Gm. ammonium carbonate, and pour into this ammoniacal solution the bismuth solution, after which ammonia water is added if the mixture is not distinctly alkaline. Let the precipitate subside, wash it several times by decantation (or by use of a syphon) with distilled water, transfer to a strainer and wash precipitate until washings are free from alkali. Then drain magma and add enough water to make 1 liter.

Magma of bismuth or *milk of bismuth* is a thick white liquid mixture that is used in diarrhea in 4 cc. doses.

Colloidal Bismuth is now prepared in a number of ways and is employed in the treatment of syphilis. For details the reader is referred to the articles listed in the bibliography found at the end of this chapter.

BISMUTHI SUBNITRAS—Bismuth Subnitrate

(Bism. Subnit.—Basic Bismuth Nitrate)

Bismuth Subnitrate is a basic salt, which, when dried to constant weight over sulfuric acid, yields upon ignition not less than 79 per cent of Bi_2O_3.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

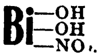
White, slightly hygroscopic powder; insoluble in water and in alcohol; soluble in hydrochloric and nitric acids, acid solution precipitates on addition of water; dissociates at red heat into nitrogen oxides and a yellow residue, that is blackened by hydrogen sulfide. For details, see U.S.P., p. 90.

For *tests for identity*, for *impurities* (alkalis and alkaline earths, ammonium compounds, insoluble foreign salts, carbonate, chloride, lead, copper, sulfate, silver, arsenic) and for *assay*, see U.S.P., p. 91.

Remarks.—An ancient synonym for this preparation was *magisterium bismuthi*, or the master of bismuth, it being considered even in the days of the alchemists as the most important preparation of that metal. It is sometimes called *flake white* (p. 608). The present Pharmacopœia gives no symbolic formula for bismuth subnitrate, as its composition varies. In the Pharmacopœia of 1880 it was said to be $BiONO_3H_2O$. The formula $BiONO_3$ can be resolved into a combination of Bi_2O_3 and bismuth nitrate, $Bi(NO_3)_3$, viz.,

$$\begin{array}{l} Bi_2O_3 \\ \underline{Bi\quad(NO_3)_3} \\ Bi_3O_3(NO_3)_3, \text{ or } 3BiONO_3. \end{array}$$

The formula $BiONO_3H_2O$ can also be considered as a combination of the hydroxide and the nitrate, viz.,



$$Bi\begin{cases}-OH\\-OH\\-NO_3\end{cases}$$

It is, therefore, apparent that the bismuth subnitrate is a mixture of the oxide and nitrate, even as ferric subsulfate is a combination of iron sulfate and iron oxide.

Hepner believes that the formula of bismuth subnitrate is more complex than those given above.

The bismuth subnitrate is prepared from bismuth nitrate, made by treatment of the metal with nitric acid, as is shown in the following equation:

$$Bi_2 + 8HNO_3 = 2Bi(NO_3)_3 + 4H_2O + N_2O_2.$$

This bismuth nitrate solution frequently contains arsenic, nearly all bismuth ores being contaminated with that metal, and in order to remove the arsenic, an elaborate process is necessary. The solution of nitrate is poured into sodium carbonate solution, when we obtain insoluble bismuth subcarbonate, while the arsenic present goes into solution in the form of sodium arsenate. The precipitate of bismuth subcarbonate is removed from the liquid by filtration, and then dissolved in nitric acid, when the nitrate is again formed. This is treated with a small quantity of water and allowed to stand twenty-four hours, when the remaining arsenic separates out in the form of crystalline bismuth subarsenate. The filtered bismuth nitrate solution is diluted with an equal quantity of distilled water, and to the mixture, water of ammonia is slowly added with constant stirring. The pure bismuth subnitrate separates out, and the precipitate is collected on the filter, washed, and dried. In the final separation of the subnitrate the real action is due to the combination of bismuth nitrate with water, as is shown by the following equation:

$$Bi(NO_3)_3 + 2H_2O = BiONO_3H_2O + 2HNO_3.$$

The function of ammonia added is to neutralize the nitric acid separated in the reaction.

At present the salt is usually made by pouring a solution of chemically pure bismuth nitrate into water.

The Pharmacopœia describes bismuth subnitrate as a heavy white powder. A special form of bismuth subnitrate, much esteemed in certain sections of the country, is a French subnitrate which occurs in the form of cones weighing 1.5 Gm., each cone being considered a medium adult dose. These cones are prepared by the process of trochiscation. (See p. 138.)

The percentage of nitric acid combined with the subnitrate is a matter of some importance as it has been found that when above 21 per cent, there is a tendency to hydrolyze when it comes in contact with water. The freed acid is then likely to produce nitrites in the intestines with untoward results. It is claimed that the effervescence of the subnitrate when it comes in contact with bicarbonates or carbonates is due to such hydrolysis.

Bismuth subnitrate is used as an astringent and tonic, although if given in large doses it acts as a sedative, and is somewhat toxic. Its action in diarrhea is largely mechanical, it forming a clammy covering for the inflamed mucous membrane, even as does prepared chalk.

Dose.—1 Gm. (15 grains).

Bismuthi Citras (U.S.P. VIII) or *Bismuth Citrate*, $BiC_6H_5O_7$, is made by heating bismuth subnitrate with citric acid and boiling for fifteen minutes, or until the test prescribed by the Pharmacopœia shows that all the subnitrate has been converted into citrate. (See below.) This process is an interesting illustration of how a chemical action not usually occurring can sometimes be produced. Ordinarily, the nitric acid combination of bismuth is much stronger than the combination of bismuth with citric acid. But if citric acid is boiled with bismuth subnitrate, it eventually drives off the stronger nitric acid by reason of the fact that the nitric acid is volatile, while the nonvolatile citric acid remains in the mixture.

Bismuth subnitrate, as mentioned above, is insoluble in ammonia water, while the bismuth citrate is quite soluble therein, and in the accepted process the boiling is continued until the precipitate is found completely soluble in ammonia water.

Bismuth citrate is an example of a salt made by the union of a trivalent metal (Bi^{III}) with a tribasic acid, $H_3C_6H_5O_7$. One atom of Bi^{III} can replace the 3 atoms of hydrogen in the citric acid, $H_3C_6H_5O_7$, and thus we get bismuth citrate, $BiC_6H_5O_7$.

Bismuth citrate is a white powder, insoluble in water or alcohol, but soluble in ammonia water with the formation of the soluble bismuth and ammonium citrate. Bismuth citrate is rarely used in medicine, and about the only reason why it was given recognition in U.S.P. VIII was because it is used in the manufacture of bismuth and ammonium citrate.

Bismuthi et Ammonii Citras (U.S.P. IX) is made by dissolving bismuth citrate in ammonia water and evaporating the filtered solution on the water bath to syrupy consistence, and scaling the same by spreading it on plates of glass.

Bismuth and ammonium citrate is in the form of small pearly scales, becoming opaque on exposure to air. It is very soluble in water and but sparingly soluble in alcohol.

In order to secure the bismuth and ammonium citrate in the form of translucent scales it is necessary to spread it very thinly on glass, and it might be worth noting that the scales of bismuth and ammonium citrate are not as handsome as are the iron scale preparations—ferric citrate, for instance. If the solution is spread thickly on glass, white, opaque scales are formed, and, as has already been noted in the official description, often the pearly scales become opaque on exposure to air. A similar statement can also be made in regard to the solution of bismuth and ammonium citrate. This forms a clear, transparent liquid when freshly prepared, but on standing it becomes cloudy, due to gradual loss of ammonia, and, as the ammonia separates, insoluble bismuth citrate precipitates out. This cloudy solution can be cleared by the addition of a few drops of ammonia water.

Bismuth citrate is used as an astringent and tonic. It will be noted that the dose is much smaller than that of bismuth subnitrate. This is due to the fact that the bismuth and ammonium citrate is a soluble product, and it must be borne in mind that when bismuth compounds are soluble, they are by no means harmless. In fact, many therapeutists deprecate the administration of soluble bismuth compounds by reason of their possible toxic action. Bismuth and ammonium citrate was the basis of the *elixir of bismuth* and the *elixir of pepsin and bismuth* of the previous edition of the National Formulary. The recipe for the latter preparation was unsatisfactory, however, because of the incompatibility of bismuth and ammonium citrate combined with pepsin. Bismuth and ammonium citrate is held in solution by alkalis and precipitated by acids and, if we add enough alkali to hold the bismuth citrate in solution, pepsin will be decomposed, while if we add an acid solution of pepsin, bismuth citrate will eventually precipitate. *Dose.*—125 mg. (2 grains).

LABORATORY EXERCISES

MAKE BISMUTH CITRATE

Recipe.—	Bismuth subnitrate	10.0 Gm.
	Citric acid	7.5 Gm.
	Distilled water, a sufficient quantity.	

Mix the bismuth subnitrate and the citric acid with 40 cc. of distilled water, and heat on a bath of boiling water, with frequent stirring, until a drop of the mixture yields a clear solution with ammonia water. Then add 500 cc. of distilled water, allow the suspended matter to deposit, wash the precipitate, first by decantation, and afterward on a strainer, with distilled water, until the washings are tasteless, and dry the residue at a gentle heat.

Chemical Explanation.—In this preparation the bismuth subnitrate is converted into bismuth citrate by boiling with citric acid, and affords an interesting illustration of the futility of the old terms, "strong acids" and "weak acids." According to that doctrine, nitric acid is a much "stronger" acid than citric acid, and yet in this case mere boiling of the subnitrate with citric acid causes the driving out of the nitric acid. This is made possible by the fact that nitric acid is a volatile substance, while citric acid is fixed; hence the boiling gives the nitric acid the opportunity for volatilizing, and the citric acid at the same time combines with the metal.

The equation of the change is as follows:

$$BiONO_3H_2O + H_3C_6H_5O_7H_2O = BiC_6H_5O_7 + HNO_3 + H_2O.$$

Complete this equation.

Calculations.—1. How much citric acid will combine with 305 Gm. bismuth subnitrate?

2. How much citric acid will combine with 10 Gm. bismuth subnitrate?

3. How much bismuth citrate can be made from 305 Gm. bismuth subnitrate?

4. How much bismuth citrate can be made from 10 Gm. bismuth subnitrate?

Remarks on Process.—*Boil the subnitrate* and citric acid with water in pint flask.

Boil until drop of mixture gives clear solution with ammonia. Both the subnitrate and the citrate are insoluble in water, but, while the subnitrate will not dissolve in ammonia water, the citrate does. Hence, when all the subnitrate is converted into citrate, the entire insoluble precipitate will dissolve in ammonia water, and as long as a part of the precipitate does not dissolve, it means that there is still some unchanged bismuth subnitrate and the boiling must be continued.

Carry out this ammonia solubility test by dipping glass rod into the mixture in flask, and then carefully immersing same into ammonia water in a test tube. The milky drops on the rod will be dissolved so soon as it is placed in ammonia if the conversion is complete. A faint turbidity, however, is permissible, since it seems practically impossible to convert the last traces of the subnitrate into the soluble citrate.

Add 500 cc. water to wash out last traces of nitric and citric acid. In this case, since the pint flask holds but 450 cc., filling the flask with water will be sufficient.

Wash precipitate by decantation, then on strainer, that is, just as you did ferric hydroxide. With the small amount made with the above quantities, collecting and washing on plain filter (6-inch paper) will suffice.

Dry residue at gentle heat—say, on top of radiator.

MAKE BISMUTH AND AMMONIUM CITRATE

Recipe.—	Bismuth citrate	10 Gm.
	Ammonia water,	
	Distilled water, each, a sufficient quantity.	

Mix the bismuth citrate with 20 cc. of distilled water and rub it to a smooth paste, heat the mixture on a water bath, and gradually add ammonia water until the salt is dissolved and the liquid is neutral or has only a faintly alkaline reaction. Then filter the solution, evaporate it on a water bath to a syrupy consistence, and spread it upon plates of glass, so that, when dry, the salt may be obtained in scales. Keep the product in amber-colored, well-stoppered bottles, protected from light.

Chemical Explanation.—As mentioned in preceding process, bismuth citrate is insoluble in water, but it does dissolve in ammonia water, forming with it a loose chemical combination, which, when scaled, is soluble in water.

Calculations.—As the combination between the bismuth citrate and the ammonia is very indefinite, no attempt will be made to work out molecular proportions.

Remarks on Process.—*Rub bismuth citrate to smooth paste,* by placing in pint evaporating dish and triturating with water, gradually added, with the pestle.

Gradually add ammonia water until the salt is dissolved—10 cc. usually suffices. An excess works no harm, since it dissipates during the evaporation. The addition of a few drops of ammonia water, from time to time during the evaporation, aids in getting a completely soluble product.

Evaporate and scale as in making ferric citrate, only spread the thin syrup *very thinly* on glass. If spread even as thin as ferric citrate, opaque scales are formed. If very thin, beautiful pearly scales result.

BISMUTHI ET POTASSII TARTRAS—Bismuth and Potassium Tartrate

(**Bism. et Pot. Tart.**—Potassium Bismuth Tartrate, Potassium Bismuthyl Tartrate)

Bismuth and Potassium Tartrate is a basic bismuth potassium bismuthotartrate, containing the equivalent of not less than 71 per cent and not more than 75 per cent of Bi_2O_3.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Granular, white, odorless powder; sweetish taste; darkens on exposure to light; soluble in about 2 parts of water; insoluble in alcohol, ether or chloroform. For details, see U.S.P., p. 87.

For *tests for identity*, for *impurities* (alcohol-soluble extractive, lead, arsenic) and for *assay*, see U.S.P., p. 88.

Remarks.—This new official bismuth is made by a method similar to the manufacture of bismuth and ammonium citrate (p. 599). It has been introduced to provide a means of obtaining the systemic effects of bismuth in the treatment of syphilis.

Dose.—0.15 Gm. (2½ grains) by parenteral injection.

Glyceritum Bismuthi (N.F. VI) is a glycerinic solution of a double tartrate of sodium and bismuth, which is soluble in both acids and alkalis and which therefore can be used with pepsin mixtures. (See p. 954.) The tartrate is a water-soluble compound which is now used in the treatment of syphilis. Also note that the Formulary gives recipes for *elixir bismuthi*, for *elixir pepsini et bismuthi* and for *elixir pepsini, bismuthi et strychninæ* (pp. 228 and 230).

BISMUTHI SUBCARBONAS—Bismuth Subcarbonate

(**Bism. Subcarb.**—Basic Bismuth Carbonate)

Bismuth Subcarbonate is a basic salt, which, when dried to constant weight at 100° C., yields upon ignition not less than 90 per cent of Bi_2O_3.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White or pale yellowish-white powder; insoluble in water or in alcohol; soluble in nitric or hydrochloric acids with effervescence; nitric acid solution is made turbid by addition of water; dissociated at red heat into water, carbon dioxide and a yellow residue of bismuth oxide. For details, see U.S.P., p. 88.

For tests for identity, for *impurities* (chlorides, lead, copper, sulfate, silver, nitrate, arsenic, alkalis, alkaline earths) and for *assay*, see U.S.P., p. 89.

Remarks.—No formula for bismuth subcarbonate is given in the present Pharmacopœia, but the standard of 1880 declared it to be $(BiO)_2CO_3$. This formula may be resolved into bismuth oxide and bismuth carbonate, as is here shown:

Bismuth oxide	$2Bi_2O_3$ or Bi_4O_6
Added to Bismuth carbonate	$Bi_2\ (CO_3)_3$
Gives	$Bi_6O_6(CO_3)_3$
Or	$3(BiO)_2CO_3$.

Bismuth subcarbonate is prepared by dissolving metallic bismuth in nitric acid, and with careful handling the resulting bismuth nitrate solution is freed from the arsenic by diluting with a little water and allowing the mixture to stand in order to permit the subarsenate to separate out. This is filtered, and to the filtered liquid an equal quantity of water is added, and then a small amount of ammonia water, when the subnitrate precipitates. The bismuth subnitrate is redissolved in nitric acid, the filtered nitrate solution is then poured into a solution of sodium carbonate, and the precipitate of bismuth subcarbonate collected on the filter, washed, and dried.

Bismuth subcarbonate is a white powder that is insoluble in water and alcohol. On exposure to light it turns yellow, hence it should be preserved in amber-colored bottles. It is used as an astringent and tonic.

Dose.—1 Gm. (15 grains).

BISMUTHI SUBGALLAS—Bismuth Subgallate

(Bism. Subgal.—Basic Bismuth Gallate, Dermatol)

Bismuth Subgallate is a basic salt, which, when dried to constant weight at 100° C., yields upon ignition not less than 52 per cent and not more than 57 per cent of Bi_2O_3.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Amorphous, bright yellow powder; insoluble in water, alcohol or ether and in very dilute mineral acids; soluble with decomposition in hydrochloric, nitric and sulfuric acids; soluble in alkaline hydroxide solutions; chars on heating and then leaves residue of bismuth oxide. For details, see U.S.P., p. 89.

For *tests for identity*, for *impurities* (lead, copper, silver, arsenic, nitrate, free gallic acid, alkalis, alkaline earths) and for *assay*, see U.S.P., p. 90.

Remarks.—This official is prepared by treating an acetic acid solution of bismuth nitrate with gallic acid. It is popularly known as *dermatol*, and is used as an astringent, both externally and internally.

Dose.—1 Gm. (15 grains).

BISMUTHI SUBSALICYLAS—Bismuth Subsalicylate

(Bism. Subsalicyl.—Basic Bismuth Salicylate)

Bismuth Subsalicylate is a basic salt, which, when dried to constant weight at 100° C., yields upon ignition not less than 62 per cent and not more than 66 per cent of Bi_2O_3.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White, or nearly white, amorphous or crystalline powder; almost insoluble in cold water; decomposed on boiling with water; partly soluble, with decomposition in hydrochloric or nitric acid; chars at red heat, finally leaving yellow residue of bismuth oxide. For details, see U.S.P., p. 91.

For *tests for identity*, for *impurities* (free salicylic acid, nitrate, lead, copper, sulfate, silver, arsenic, alkalis, alkaline earths) and for *assay*, see U.S.P., p. 92.

Remarks.—Bismuth subsalicylate is made by triturating and warming an aqueous solution of salicylic acid with anhydrous bismuth oxide, obtained by boiling bismuth hydroxide which has been prepared by precipitating a nitric acid solution of bismuth subnitrate with potassium hydroxide or ammonium hydroxide. It is used as an intestinal antiseptic.

Dose.—1 Gm. (15 grains) by mouth; 0.125 Gm. (2 grains) parenterally as an anti-syphilitic.

Bismuthi Tribromphenolas (N.N.R.) or *Xeroform*, $(C_6H_2Br_3O)_2.Bi(OH).Bi_2O_3$, is an amorphous yellow powder, used as a nonirritant and nontoxic antiseptic.

Bismuth Therapy.—During the past ten years, considerable attention has been paid to the use of bismuth compounds in syphilis. The antisyphilitics are grouped by Dyson as follows: (*a*) suspensions of colloidal bismuth in an aqueous saline or an oily medium, (*b*) solutions of a true organo-bismuth compound in an organic medium, (*c*) water-soluble bismuth compounds such as bismuth sodium tartrate, (*d*) suspensions of water-insoluble bismuth compounds in aqueous or oily media.

BIBLIOGRAPHY

Cadmium.—(Discovery) Strohmeier, Jl. de ph., 4, 1818, 288. (Production) Anon., Jl. Soc. Ch. Ind., 49, 1930, 737. (Technical uses), Anon., Jl. Soc. Ch. Ind., 47, 1928, 316; Budgen, C. A., 23, 1929, 2370. (Medical uses) Cooper and co-workers, Jl. Soc. Ch. Ind., 45, 1926, 321 C.A., and 49, 1930, 388T.

Copper.—(History) De Launay, Rev. gen. sci., 19, 1909, 449; Dioscorides, Lippmann, Zt. angew. Ch., 18, 1905, 1211; Hackh, A.J.P., 90, 1918, 490; Dyson, Ph. Jl., 125, 1930, 31; Pines, A.J.P., 104, 1932, 613. (Sources) Poste, Jl. Ind. Eng. Ch., 24, 1932, 690. (Metallurgy) Anon., Eng. Min. Jl., 104, 1917, 691. (Properties) Anon., Bur. Standards Circ., 73, 1922, 1; Greenwood, Ch. News, 104, 1912, 31 and 42.

Flotation.—Durell, C.A., 10, 1916, 1153; Motherwell, C.A., 11, 1917, 327; Gibbs, Jl. Soc. Ch. Ind., 48, 1929, 135; Gaudin, C.A., 25, 1931, 4497; Miller and Kidd, C.A., 25, 1931, 5371; O'Meara and co-workers, C.A., 25, 1931, 3281; Kamienski, C.A., 26, 1932, 53; Ostwald, C.A., 26, 1932, 2946; Siedler and co-workers, C.A., 26, 1932, 5884.

Bronze.—Dewrance, Engineering, 97, 1914, 405 and 412; Strauss, C.A., 22, 1928, 747.

Phosphor-bronze.—Sperry, Brass World, 3, 1909, 399; Glaser and Seemann, Jl. Soc. Ch. Ind., 45, 1926, 411B; Thormann, C.A., 24, 1930, 4497.

Japanese Bronze.—Karr, Brass World, 10, 1914, 93.

Manganese Bronze.—Corse and Skillman, Met. Ch. Eng., 12, 1914, 113.

Monel Metal.—Arnot, C.A., 13, 1919, 220.

Cuprammonium Compounds.—Horn and Taylor, Am. Ch. Jl., 32, 1904, 253.

Copper Oxides.—(Composition) Bailey and Hopkins, Jl. Ch. Soc., 57, 1890, 269; Moser, Zt. anorg. Ch., 64, 1909, 200.

Copper Sulfate.—(History) Wootton, 1, 1910, 372; Sala (1647) through Kopp, 1, 1843, 116. (Manufacture) Baskerville, Jl. Am. Ch. Soc., 17, 1895, 904 and 18, 1896, 942; Cundall and Fairgrieve, Jl. Ch. Soc., 105, 1914, 60; Matsuno, C.A., 17, 1923, 3405. Rogers, C.A., 20, 1926, 1363. (Water of hydration) Kay, Ch. News., 141, 1930, 70; Smith and Topley, C.A., 26, 1932, 2638; Logan, C.A., 26, 1932, 2640. (Technical uses) Anon., A.Ph.A., 58, 1910, 274; Drew, Jl. Soc. Ch. Ind., 47, 1928, 212.

Paris Green.—Avery, Jl. Am. Ch. Soc., 28, 1906, 1155.

Verdigris.—(History) Kopp, 4, 1847, 339.

Bismuth.—(History) Husemann, A.J.P., 72, 1900, 345; Hackh, A.J.P., 90, 1918, 478; Dyson, Ph. Jl., 120, 1928, 242 and 582. (Atomic weight) Classen and Ney, C.A., 15, 1921, 1643. (Occurrence and properties) Anon., C.A., 24, 1930, 3610; Tyler, C.A., 25, 1931, 4827. (Melting point) Anon., Ch. News, 118, 1921, 129.

Fusible Alloys.—Bauer and Schack, Jl. Soc. Ch. Ind., 43, 1924, 521B; Horn, A.J.P., 100, 1928, 558.

Colloidal Bismuth.—Gutbier and Kantter, Jl. Soc. Ch. Ind., 44, 1925, 737B; Kuhn and Pirsch, C.A., 20, 1926, 1010; Parnell, C.A., 20, 1926, 1270.

Bismuth Subnitrate.—(History) Raubenheimer, Merck's Rep., 19, 1910, 156. (Structure) Hepner, Arch. d. Pharm., 264, 1926, 55. (Manufacture) Procter, A.J.P., 36, 1864, 302. (Hydrolysis) Dunning, Dr. Circ., 53, 1909, 331; Lion, Gaz. med. Paris, 80, 1909, 5; Zadek, C.A., 9, 1915, 658; Ionescu, *ibid.*, 15, 1921, 120. (Therapeutics) Stieglitz, C.A., 27, 1933, 139.

Bismuth Oxide.—Muir., Jl. Ch. Soc., 29, 1876, 149 and 32, 1877, 128; Muir and Hutchinson, Jl. Ch. Soc., 55, 1889, 143.

Bismuth Hydroxide.—Raubenheimer, A.Ph.A., 57, 1909, 1025.

Bismuth Citrate.—Rother, A.J.P., 48, 1876, 105; Bartlett, A.J.P., 37, 1865, 1; Adams, Ph. Jl., 113, 1924, 87; Morton, Quart. Jl. Ph., 3, 1930, 562.

Bismuth Subcarbonate.—Tapley and Giesy, Jl. A.Ph.A., 15, 1926, 46.

Bismuth and Sodium Tartrate.—Yoe and Mote, Jl. A.Ph.A., 18, 1929, 450; Morton, Quart. Jl. Ph., 4, 1931, 1; Kober, C.A., 26, 1932, 2505.

Scale Bismuth Salts.—Feil, A.Ph.A., 35, 1887, 617.

Bismuth and Ammonium Citrate.—Rother, A.J.P., 48, 1876, 105; Bartlett, A.J.P., 37, 1865, 2.

Bismuth Subgallate.—(History, composition and properties) Kebler, A.J.P., 71, 1899, 326; Fischer, A.Ph.A., 40, 1892, 1018; Fischer, Ph. Zt., 36, 1891, 490; Anon., Ph. Zt., 36, 1891, 386; Teletov, Ph. Cent., 70, 1929, 61.

Bismuth Subsalicylate.—Fischer, A.Ph.A., 43, 1895, 674.

Bismuth Therapy.—Dyson, Ph. Jl., 120, 1928, 582.

CHAPTER XXXIV

LEAD, MERCURY, AND SILVER

LEAD

Symbol, Pb. Atomic weight, approximately 207

LEAD occurs in the form of sulfide in the ore *galena*. By way of passing it is worth noting that some galena ore contains considerable silver. (See p. 622.) Among the other ores of lead are various forms of the carbonate and the sulfate.

Metallic lead was used in classic times, the Latin name *plumbum* being applied to it by classic writers, its original meaning being "heavy."

Lead is prepared from the sulfide by roasting in a reverberatory furnace, thus converting the sulfide, under the influence of atmospheric oxygen, into lead oxide and lead sulfate, shown in the following equations:

$$PbS + O_3 = PbO + SO_2.$$
$$PbS + O_4 = PbSO_4.$$

The resulting lead oxide combines with a new portion of lead sulfide with the formation of the metal and the separation of SO_2 by the following equation:

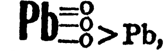
$$2PbO + PbS = Pb_3 + SO_2,$$

while the lead sulfate reacts with more lead sulfide in the manner shown in the following equation:

$$PbSO_4 + PbS = Pb_2 + 2SO_2.$$

Lead is a heavy, bluish metal, freely malleable, and somewhat ductile. Its pliability has given rise to its extended use in plumbing, the name of the craft being derived from the word *plumbum*, lead, since leaden pipes are largely used for the transport of water. It should be said that lead water pipes are scarcely harmless, traces of lead hydroxide dissolving, and water so contaminated produces a dangerous ailment called lead colic. With hard water, *i. e.*, water containing lime and magnesia dissolved by aid of carbon dioxide, there is less danger, as carbonic acid acts on fresh lead, forming lead carbonate, which coats the interior of the pipe and prevents any of the lead dissolving in the water. Lead is used in the manufacture of *solder*, which is a variety of the fusible metal made by combining equal quantities of tin and lead. This mixture melts at 186° C., and is used for fastening pieces of tin or other metal together.

The *tests* for lead are as follows: hydrochloric acid produces a white precipitate of lead chloride, being one of the three chlorides thus precipitated, the other two metals precipitating in the form of chloride being silver and mercurous compounds. Lead gives with hydrogen sulfide and ammonium sulfide a black sulfide; with sulfuric acid it precipitates white lead sulfate, and with carbonates, white lead carbonate is precipitated out of the solution. Quite characteristic is the yellow precipitate of lead chromate produced when a solution of lead salt is treated with a solution of potassium chromate.

Four oxides of lead are known, PbO, or *litharge*, U.S.P.; Pb_2O_3, which may be considered as a mixture of PbO and PbO_2, the composition of which can best be explained by the following graphic formula,  $Pb{=O \atop {-O \atop -O}}{>}Pb$, that is, a combination of lead with valence IV, with lead with valence II; PbO_2, which is called *puce-colored lead oxide*, in which lead shows valence iv; Pb_3O_4, or *red lead* (N.F. V), which can be considered as a combination of Pb_2O_3 and PbO, or else as a lead plumbate, Pb_2PbO_4; that is, the lead salt of orthoplumbic acid, $Pb(OH)_4$ or H_4PbO_4. Red lead is made by sprinkling hot litharge with water and carefully drying. It is of value as a pigment. What was formerly called lead suboxide, Pb_2O, is declared by Van Arkel to be a mixture.

The official preparations of lead are:

Lead acetate. At least 99.5 per cent $Pb(C_2H_3O_2)_2.3H_2O$.

Solution of lead subacetate (N.F. VI). Contains lead subacetate, $Pb_2O(CH_3COO)_2$ corresponding to at least 22.5 per cent lead.

Lead monoxide (N.F. VI). At least 97 per cent absolute PbO.

Lead oleate plaster (N.F. VI). A lead oleopalmitate.

Diachylon ointment (N.F. VI) contains 50 per cent lead plaster.

Plumbi Monoxidum (U.S.P. X; N.F. VI), or *Lead Monoxide*, is also called *litharge*, a word used since ancient times, and derived from the two Greek words, *lithos*, a stone, and *arguros*, silver. It is so called because the ancients discovered that when the ore, crude litharge, was fused, the pure litharge, freed from the mineral impurities, fused in the form of bright, shiny, silvery scales. It is a heavy yellowish or reddish yellow powder almost insoluble in water.

The chief source of litharge is as a side-product in obtaining silver from galena. The ore (lead sulfide, p. 604) is calcined, thus driving off the sulfur, and the residue brought to a state of fusion, when the lead oxide separates out by crystallization from the fused mass of silver.

Litharge is but little used in medicine, although important as a constituent of two popular pharmaceuticals, *solution of lead subacetate* (N.F. VI) and *lead plaster* (N.F. VI).

PLUMBI ACETAS—Lead Acetate

(Plumb. Acet.—Sugar of Lead)

$Pb(C_2H_3O_2)_2.3H_2O$. Molecular weight, 379.31

Lead Acetate contains not less than 85.31 per cent and not more than 89.57 per cent of $(CH_3.COO)_2Pb$, corresponding to not less than 99.5 per cent of the hydrated salt $(CH_3.COO)_2Pb.3H_2O$.

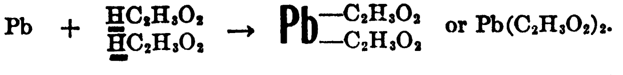
Storage.—Preserve in air-tight containers.

Summarized Description.

Colorless, shining, efflorescent, monoclinic prisms or plates, or heavy white crystalline masses or granular crystals; faintly acetous odor; sweetish, astringent, then metallic taste; soluble in about 1.6 parts of water and in about 24 parts of alcohol; quite soluble in glycerin; on heating is exsiccated, then fuses and then dissociates. For details, see U.S.P., p. 293.

For *tests for identity*, for *impurities* (carbonate, iron and copper alkalis and alkaline earths), see U.S.P., p. 294.

Remarks.—Lead acetate is incorrectly and dangerously called "*sugar of lead.*" Lead being bivalent, it can replace 2 hydrogen atoms in an acid, and since acetic acid has but one replaceable hydrogen atom to the molecule, 2 molecules of acetic acid are needed to combine with 1 atom of lead, thus:



$$\mathrm{Pb} + \begin{matrix}\underline{\mathrm{H}}\mathrm{C_2H_3O_2}\\ \underline{\mathrm{H}}\mathrm{C_2H_3O_2}\end{matrix} \rightarrow \mathrm{Pb}\begin{matrix}-\mathrm{C_2H_3O_2}\\ -\mathrm{C_2H_3O_2}\end{matrix} \text{ or } \mathrm{Pb(C_2H_3O_2)_2}.$$

However, the acetate is usually made by treating the oxide, litharge, (*not the metal*) with acetic acid.

The solution is concentrated, and the lead acetate is allowed to crystallize. It is important to note that the average commercial lead acetate should not be dispensed without purification, as it contains appreciable quantities of both lead oxide and lead carbonate. The purification of this commercial lead acetate is a simple matter, however, the acetate dissolving in water and recrystallizing, while the impurities do not dissolve.

Lead acetate is used as an astringent and sedative, both internally and externally. An overdose acts as an irritant poison, producing severe gastric disturbances. The antidote for lead poisoning or in lead colic is an alkaline sulfate, the one generally preferred being magnesium sulfate or Epsom salt. Externally, lead acetate is used either in an aqueous solution or in the form of suppositories, the latter being a highly esteemed remedy for piles, a favorite prescription of this kind being lead acetate with extract of opium and oil of theobroma.

The preparation of the suppositories of lead and opium requires considerable skill. The extract of opium should be rubbed up with enough water to make it into a paste thin enough to pour. The lead acetate should be reduced to the form of an impalpable powder, and added to the molten oil of theobroma, with constant stirring, the mixture is then poured into molds, after adding the thinned extract, just at that moment when the oil of theobroma is ready to solidify. Unless these precautions are followed (especially the stirring), there is danger of the heavy lead acetate settling at the bottom of the dish in which the oil of theobroma is melted, and thus the last suppository poured therefrom will contain a majority of the lead salt.

Lead acetate solution is used as a wash for some skin troubles, such as ivy poisoning and chilblains, but for this purpose a solution of lead subacetate is frequently preferred.

Liquor Plumbi Subacetatis (N.F. VI), or *Solution of Lead Subacetate*, or *Goulard's Extract* contains lead subacetate, which, like all "sub-"salts (see Ferric Subsulfate, p. 570), is a combination of a salt of a metal with the oxide of the same metal. Remember it is not a mere mechanical mixture, but a combination like that existing between the sulfates of aluminum and potassium in official alum.

The solution is made by boiling together water, lead acetate, and lead oxide, full details of manufacture and equation, showing chemical action, being given below. The Formulary says that the solution contains approximately $Pb_2O(C_2H_3O_2)_2$, which we find corresponds to the sum resulting from the addition of one molecule of lead acetate to one molecule of lead oxide, viz.:

$$\begin{array}{ll} Pb\ (C_2H_3O_2)_2 & \text{(Lead acetate.)} \\ Pb\,O & \text{(Lead oxide.)} \\ \hline Pb_2O(C_2H_3O_2)_2 & \text{(Lead subacetate.)} \end{array}$$

That a chemical change is produced is shown by the fact that the insoluble lead oxide is made to dissolve with the formation of a soluble oxyacetate.

It will be noted that the lead subacetate solution is unstable, unless kept tightly corked, the carbon dioxide of the air acting on the solution, with the formation of lead carbonate which precipitates.

Solution of lead subacetate is used almost entirely externally; for this purpose being employed as a sedative and astringent wash in minor skin troubles, such as bruises, frost-bite, and the like. For many purposes of this kind a diluted solution is preferable, and that is provided by the Pharmacopœia.

Morton believes that the lead complex in Goulard's extract is $PbO.Pb(C_2H_3O_2)_2.H_2O$.

LABORATORY EXERCISE

MAKE SOLUTION OF LEAD SUBACETATE

Recipe.—Lead acetate	18 Gm.
Lead oxide	11 Gm.
Distilled water a sufficient quantity,	
To make	100 Gm.

To the finely powdered lead oxide contained in a porcelain dish of about half-liter capacity, add slowly and in portions, with constant stirring, the lead acetate which has been previously dissolved in 70 cc. of boiling distilled water, and boil the liquid for half an hour, with occasional stirring. Finally, when cool, filter the solution, and add sufficient distilled water, which has been previously boiled and cooled, to make the finished product weigh 100 Gm. Keep the solution in well-stoppered bottles.

Chemical Explanation.—As explained on p. 570, a "sub-"salt is a basic salt—that is, a combination of a salt of a metal with the oxide of the same metal.

In the preparation under consideration the "sub-"salt is made by direct combination of the salt and the oxide, lead acetate and lead oxide being boiled together with the formation of lead subacetate, as shown in the following equation:

Lead acetate	plus	Lead oxide	give	Lead subacetate	plus	Water
$Pb(C_2H_3O_2)_2.3H_2O$	+	PbO	=	$Pb_2O(C_2H_3O_2)_2$	+	$3H_2O$.
(Soluble.)		(Insoluble.)		(Soluble.)		

Calculations.—Figure out molecular weights of the three lead preparations given above, and from these figures work out the following examples:

1. How many grams lead acetate needed to make 548 Gm. lead subacetate?
2. How many grams lead acetate needed to make 25 Gm. lead subacetate?
3. How many grams lead oxide needed to make 548 Gm. lead subacetate?
4. How many grams lead oxide needed to make 25 Gm. lead subacetate?
5. How many grams lead subacetate in 100 Gm. solution of lead subacetate which is 25 per cent subacetate?
6. Then how many grams of lead subacetate and lead oxide needed to make 100 Gm. solution of lead subacetate?

Remarks on Process.—The recipe just given is substantially the recipe of U.S.P. IX. U.S.P. X directs preparation upon a weight-volume basis using 220 Gm. lead acetate and 140 Gm. lead oxide to 1000 cc. of finished solution. The rubric of N.F. VI directs 22.5 per cent lead (weight-volume) which corresponds to the old strength of about 25 per cent, by weight, lead subacetate.

Dissolve lead acetate in pint flask.

Pass the lead oxide through a No. 80 sieve before weighing, then put into tared pint evaporating dish.

Boil mixture one-half hour, during which time a large amount of the insoluble lead oxide passes into the soluble lead subacetate.

All the lead oxide will not dissolve, however, and that is the reason an excess over the theoretic amount is directed in official recipe.

Add hot water to make up the loss of evaporation, otherwise the mixture will evaporate to dryness during the half hour's boiling.

Make finished product weigh 100 Gm. by adding enough *freshly boiled* water. Even distilled water contains carbon dioxide if allowed to stand, and this carbon dioxide will precipitate the lead as lead carbonate; so boil the water to drive off the dissolved carbon dioxide before using it as a diluent.

Filter in closely covered funnel and keep in well-stoppered bottles to prevent atmospheric action. The air contains carbon dioxide, and this precipitates the lead, as mentioned above.

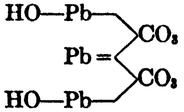
Liquor Plumbi Subacetatis Dilutus (N.F. VI), or *Lead Water*, is made by diluting 35 cc. of the stronger solution of lead subacetate (see above) with 965 cc. of water, which has previously been boiled in order to expel the carbon dioxide it might contain. (See p. 212.) This solution is usually dispensed in a slightly opalescent condition, first because, on standing, it will gradually become opalescent anyway, and, secondly, to afford a differentiation between the so-called "lead water" and "lime water," the latter product being dispensed in a crystal-clear form.

Lead water is used as a soothing lotion, and is frequently dispensed in combination with a small quantity of tincture of opium. This mixture, while quite popular, is incompatible, for, as soon as the tincture of opium is added to the lead water, there is formed a flocculent precipitate (lead meconate). The prescription is a usual one, however, and pharmacists always dispense the same, containing the precipitate, placing a "Shake Well!" label on the bottle.

Ceratum Plumbi Subacetatis (N.F. VI), or *Cerate of Lead Subacetate*, is made by incorporating solution of lead subacetate with an ointment base consisting of wool fat, white wax, white petrolatum, and camphor. It, like the solution from which it is made, was first introduced by the surgeon Goulard, hence it is called *Goulard's cerate*. Goulard's cerate is used for mild skin troubles, and is particularly recommended for cases of chilblain.

Plumbi Carbonas (U.S.P. 1890; N.F. IV), like the carbonates of zinc and of magnesium, is a combination of the carbonate and the hydroxide; the formula given the compound in the Pharmacopœia of 1890 having been $(PbCO_3)_2Pb(OH)_2$.

It must be borne in mind that such a formula as the one just given does not represent a mechanical mixture of lead carbonate and lead hydroxide, but a combination far more intimate, which may be best explained by the following graphic formula:



Falk claims that the formula is more complex, that is, $5PbCO_3 2Pb(OH)_2 PbO$; while Euston considers it as a mixture of $PbCO_3.Pb(OH)_2$ and $PbCO_3$.

Lead carbonate can be made in small quantities at the prescription counter by combination of molecular quantities of lead nitrate and sodium carbonate, but that used for paint is produced by other means. The oldest method and one still largely used, because of the superiority of the product, as a paint, is that made by the so-called *Dutch process*. By this process sheets of lead are boiled in earthenware pots, moistened with acetic acid. A long series of these pots, carefully covered to prevent the admission of dirt, and yet loose enough to permit the admission of gases, are then placed in rows, are covered with decaying tan yard refuse, and allowed to stand so covered for five to six weeks. The decaying animal matter produces a large quantity of carbon dioxide, which is gradually absorbed by the lead acetate first produced in the pots by the action of acetic acid on the sheet lead. Experience tells how long the maceration should continue, and when a sufficient length of time has elapsed, the coverings are removed, and the contents of the pots are found to consist of powdered white lead. Besides this Dutch process, large quantities of white lead are now made for paints by passing carbon dioxide through a solution of lead subacetate.

Lead carbonate is usually called *white lead.* Like bismuth subnitrate (p. 598) it is sometimes called *flake white.*

Lead carbonate is indicated in some cases of skin trouble and is then usually applied in the form of ointment (*unguentum plumbi carbonatis*, U.S.P. 1890). This consists of 10 Gm. of lead carbonate in a very finely powdered form, rubbed up with 90 Gm. of benzoinated lard.

A considerable amount of white lead was formerly used as a cosmetic (face powder). Its use for this purpose is dangerous, because of the absorption of the lead through the pores of the skin, causing lead colic.

Rubbed to a fine paste with linseed oil, white lead constitutes one of the most popular white paints, although such paints should not be used in lavatories or other apartments where there is a possibility of the liberation of hydrogen sulfide gas, which will change the white lead carbonate into the black lead sulfide.

Plumbi Iodidum (U.S.P. VIII; N.F. V), or *Lead Iodide*, PbI_2, shows lead with valence, II, the linkage being,

$$Pb\begin{matrix}-I\\-I\end{matrix}$$

This chemical is made by treating a solution of lead nitrate with potassium iodide, as shown in the following equation,

$$Pb(NO_3)_2 + 2KI = PbI_2 + 2KNO_3,$$

and collecting and washing the precipitated lead iodide.

Lead iodide is rarely used internally. When it is, it acts as an alterative, and is given in doses of 1 to 3 grains. Its chief value is for external use in tumors and indolent swellings, in which case it is usually employed in the form of the *unguentum plumbi iodidi* (N.F. V), which is made by rubbing up 10 parts of very finely powdered lead iodide with 90 parts of benzoinated lard.

Plumbi Nitras (U.S.P. VIII) or *Lead Nitrate*, $Pb(NO_3)_2$, is made by treating lead oxide with nitric acid, as shown in the following equation:

$$PbO + 2HNO_3 = Pb(NO_3)_2 + H_2O.$$

The solution of lead is concentrated by the evaporation of the surplus water, and after filtering it is allowed to stand, when the lead nitrate separates in the form of small crystals.

The use of lead nitrate is for the preparation of the other salts of lead. Medicinally, it is used externally as a cooling wash, and enjoys some reputation as a disinfectant.

Emplastrum Plumbi Oleatis (N.F. VI), or *Lead Oleate Plaster*.

For recipe, see below.

This is an oleopalmitate of lead prepared by boiling olive oil and lard with a mixture of lead oxide and water. The chemistry of the process is discussed on the next page. In the U.S.P. VIII lead plaster was prepared by precipitating a solution of soap with a solution of lead acetate, but the product was not wholly satisfactory.

As the name indicates, the product is used as a plaster base.

LABORATORY EXERCISES

MAKE LEAD PLASTER (N.F. VI)

Recipe.—	Lead oxide	16 Gm.
	Olive oil	16 Gm.
	Lard	16 Gm.
	Water, a sufficient quantity.	

Sift the lead oxide through a No. 80 sieve into the melted fats contained in a bright copper boiler of a capacity equal to at least four times the bulk of the ingredients. Then add 6 cc. of boiling water, and boil the whole together, over a fire, constantly stirring with a wooden spatula, until a small portion, when dropped into cold water, is found to be pliable and tenacious. From time to time add a little water to replace that lost by evaporation. When the contents of the boiler have acquired a whitish color and are perfectly homogeneous, transfer them to a vessel containing warm water, and as soon as the mass has sufficiently cooled, wash it well with the water so as to remove the glycerin, renewing the water from time to time, as long as it may be necessary. Finally, knead the mass until free from water and divide into rolls of suitable size.

Chemical Explanation.—As learned on p. 742 when an oil—which is the combination of glycerin with oleic acid and other acids—is treated with the hydroxide of a metal, glycerin is set free and a metallic oleate is formed. Thus, if an oil is treated with soda (NaOH), sodium oleate or hard soap is formed; if the same oil is treated with potassa (KOH), potassium oleate or soft soap is obtained.

Therefore, when olive oil is boiled with lead oxide in the presence of water (thus forming lead hydroxide, viz., $PbO + H_2O = Pb(OH)_2$), lead oleate is produced by the following equation:

Olive oil (Olein) (Glyceryl oleate)	plus	lead hydroxide	give	lead plaster	plus	glycerin
$C_3H_5(C_{18}H_{33}O_2)_3$	+	$Pb(OH)_2$	=	$Pb(C_{18}H_{33}O_2)_2$	+	$C_3H_5(OH)_3$.

Complete this equation.

The result of the reaction is a viscid mass consisting chiefly of lead oleate, and called lead plaster, and by kneading this lead plaster with water the glycerin is removed.

As the olive oil contains traces of glyceryl palmitate and glyceryl stearate the finished plaster contains some lead palmitate and lead stearate; hence it is not a definite chemical.

Calculations.—Since we are not dealing with definite chemicals, the molecular proportions of this reaction cannot be easily worked out; hence they are omitted.

Remarks on Process.—The recipe just given is similar to but not identical with that given in the present edition of the Formulary. The two recipes should be carefully compared by the student.

Sift the lead oxide upon the melted fats and then add the water.

The *plaster should be cooked in a copper boiler*, since the lead is apt to attack glass or porcelain, dissolving off some. For the small amount we are making, however, the pint evaporating dish may be used.

Boil mixture in dish over Bunsen burner flame on wire gauze, stirring with wooden paddle. Both glass rod and steel spatula are taboo—the first for fear the lead might attack it; the steel spatula lest the oleic acid attack it.

Replace water lost by evaporation, and that only cautiously, adding boiling hot water. The temperature of the boiling plaster mass is considerably above 100° C., and if cold water is added, steam will be developed with explosive suddenness, spattering the hot plaster mass in all directions, and rendering the operator liable to severe burns.

The *mass is finished* when a drop solidifies in water.

After washing out the glycerin from the finished mass the glycerin may here covered from the water solution—from the wash water—by evaporating off the water at very low heat. Use hydrant water for the washing.

Lastly knead out the water (a sticky job!), and divide into rolls.

MAKE LEAD PLASTER (U.S.P. VIII)

Recipe.—	Soap, dried, and in coarse powder	10 Gm.
	Lead acetate	6 Gm.
	Water, a sufficient quantity.	

Dissolve the soap in 35 cc. of hot water and strain the solution. Dissolve the lead acetate in 25 cc. of hot water, and at once filter the solution into the warm soap solution, stirring constantly.

When the precipitate has subsided, decant the liquid, and wash the precipitate thoroughly with hot water. Transfer the mass to a warm slab, kneading it thoroughly to free it from water. Finally, roll the plaster into cylindric forms and wrap them in paraffined paper.

Chemical Explanation.—This type of lead plaster, recognized in U.S.P. VIII, is typical of the line of solid oleates (or, more correctly, oleopalmitates) such as those of zinc and of copper. These are made by mixing a solution of castile soap (sodium oleate and sodium palmitate) with a solution of salt of the metal desired. In the case of lead plaster (U.S.P. VIII) the reaction runs:

Sodium oleate plus *lead acetate* give *lead oleate* plus *sodium acetate.*

Write out the equation showing this reaction.

As neither Castile soap nor lead plaster are definite chemicals, no attempt will be made to calculate quantities by molecular weights.

Remarks on Process.—*Dissolve the soap* in pint flask, and strain into pint evaporating dish.

Dissolve the lead acetate in another pint flask (or same one, carefully washed), and filter into soap solution in dish.

Knead the mass on pill tile.

Unguentum Plumbi Oleatis (N.F. VI) or *Ointment of Lead Oleate* or *diachylon ointment* consists of melted lead plaster diluted with white petrolatum and flavored with oil of lavender. (See p. 371.) The ointment was formerly in considerable repute as a remedy for eczema.

MERCURY

Symbol, Hg. Atomic weight, 200.6

Mercury occurs chiefly as a sulfide, forming the valuable mineral *cinnabar,* and is occasionally found in the native state. Cinnabar has been known since the time of the Grecian philosophers, and the separation of the metal by heating of cinnabar was described by Dioscorides, while the metal was called hydrargyrum (water silver) by Pliny. It was first used in medicine by Paracelsus.

Metallurgy.—Mercury is obtained by roasting cinnabar in an appropriate retort, when mercury and sulfurous oxide are formed, as shown in the following equation:

$$HgS + \underset{\left(\substack{\text{From the}\\ \text{air}}\right)}{O_2} = Hg + SO_2.$$

The vapors of sulfurous oxide are permitted to escape, while the metallic mercury is held back in an appropriate condenser.

Mercury is a silvery white, mobile liquid, hence called *quicksilver.* It has a specific gravity of 13.5, and is the heaviest known liquid. It is, moreover, of interest as being the only metallic substance which is liquid at ordinary temperatures. It requires a cold of almost 40° C. below zero (either Fahrenheit or Centigrade) to solidify it.

Mercury has the property of combining with almost all the metals (but iron), forming liquid alloys, which we call amalgams; some of which are definite chemical compounds (example, KHg). The fact that iron does not combine with mercury permits the storage of mercury in iron containers. Mercury boils at about 350° C., but vaporizes below that temperature, and the vapor is poisonous. Hence trades demanding the use of a large amount of mercury, such as in making mirrors, are dangerous to the health of the workmen. As mentioned on p. 387 the atomic and molecular weight of mercury is the same, 200.

Dental Amalgam consists of silver, tin, and sometimes copper made into a plastic mass by the addition of mercury. According to Sellner the "set" amalgam in the filled cavity is largely the alloy AgHg. There has lately been some controversy as to the possibility of danger to the health by the use of such dental amalgams.

The *tests* for mercury are as follows: the black sulfide produced by the action of hydrogen sulfide or ammonium sulfide; a routine test, which is of very little value, except in the precipitation of mercury in the regular scheme of analytic chemistry. (See p. 1002.) In this test both forms of mercury (the "ous" and "ic") separate in the form of black mercuric sulfide. There are quite a number of characteristic tests differentiating the "ous" compounds from the "ic" compounds. The potassium iodide precipitates from the solution of mercurous salts the yellow mercurous oxide; while the same reagent with the mercuric salts gives a red mercuric iodide. Hydrochloric acid precipitates from solutions of mercurous salts insoluble white mercurous chloride; while with "ic" salts no precipitate is formed by this reagent. Metallic copper or stannous chloride solution, when mixed with a mercurous compound, reduces it to a metallic mercury, which separates out in the form of a fine gray precipitate. Calcium hydroxide solution (lime water) forms with mercurous compounds a black precipitate of mercurous oxide—Hg_2O—and the liquid so prepared from calomel water and lime water is called *black wash* (*aqua phagedœnica nigra, lotio nigra,* N.F.). Mercuric salts with lime water form a yellow precipitate of mercuric oxide, and a liquid so prepared from corrosive sublimate water and lime water is called *yellow wash* (*aqua phagedœnica flava, lotio flava,* N.F.).

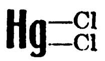
Two oxides of mercury are known—Hg_2O, mercurous oxide, and HgO, mercuric oxide.

Referring to the table of elements on p. 390, we find that mercury is both univalent and bivalent, and we, therefore, have two lines of mercury salts—the mercuric and mercurous.

When speaking of copper on p. 595, attention was called to the fact that that metal exhibited the valence I and II, and that such variation did not agree with the now exploded theory, that variation in valence should be by twos. Such exception we found in the ferric and ferrous salts, the apparent valence in that case being II and III, and that exception was explained on p. 558 by the theory that ferric iron really has the valence IV, making iron, II and IV. In a somewhat similar way we explain the valence of copper and mercury. In the mercuric form the valence is undoubtedly II, and mercuric chloride can be expressed as shown in Formula A, given below.

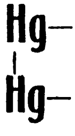
In the mercurous form the valence is also supposed to be II, and all mercurous compounds are supposed to be made up of 2 atoms of mercury linked as in Formula B. Thus we suppose the formula of mercurous chloride (calomel) is as in Formula C,

FORMULA A



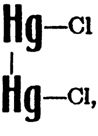
$$\mathrm{Hg}\begin{array}{l}-\mathrm{Cl}\\-\mathrm{Cl}\end{array}$$

FORMULA B



$$\begin{array}{l}\mathrm{Hg}-\\ \mid\\ \mathrm{Hg}-\end{array}$$

FORMULA C



$$\begin{array}{l}\mathrm{Hg}-\mathrm{Cl}\\ \mid\\ \mathrm{Hg}-\mathrm{Cl},\end{array}$$

and the Pharmacopœia of 1890 gave the formula of calomel as Hg_2Cl_2, not $HgCl$, and likewise with all other mercurous salts.

The theory of the bivalency of mercury in mercurous compounds is not, however, unanimously accepted, some chemists considering mercury in the "ous" form as possessing valence I, and thus giving the mercurous bodies the simpler single formula—for example, calomel, $HgCl$. This view is the one recognized in the present Pharmacopœia where all formulas (see Alum, p. 546 and Ferric Chloride, p. 565) are given their simplest form.

The official forms of mercury and its compounds are:

Mercury. At least 99.5 per cent absolute Hg.
Mass of mercury contains from 32 to 34 per cent mercury.
Mild mercurial ointment contains about 30 per cent mercury.
Stronger mercurial ointment contains about 50 per cent mercury.
Mercury with chalk contains from 37 to 39 per cent mercury.
Ammoniated mercury—$HgNH_2Cl$—contains 78 to 80 per cent mercury.
Ointment of ammoniated mercury contains 10 per cent ammoniated mercury.
Mercury bichloride. At least 99.5 per cent absolute $HgCl_2$.
Poison tablets of corrosive mercuric chloride (two sizes).
Mild mercurous chloride. At least 99.6 per cent absolute HgCl,
Red mercuric iodide (N.F. VI). At least 99 per cent absolute HgI_2.
Yellow mercurous iodide. At least 99 per cent absolute HgI.
Yellow mercuric oxide. At least 99.5 per cent absolute HgO.
Ointment of yellow mercuric oxide contains 1 per cent yellow mercuric oxide.
Mercuric salicylate contains from 54 to 59.5 per cent of mercury combined as salicylate.
Mercuric succinimide contains from 49.5 to 51 per cent of mercury. (See p. 683.)

HYDRARGYRUM—Mercury

(Hydrarg.—Quicksilver)

Symbol, Hg. Atomic weight, 200.61

Mercury contains not less than 99.5 per cent of Hg.

Storage.—Preserve in strong, well-closed containers.

Summarized Description.

Shining silver-white, liquid metal; easily divisible into spherical globules; solidifies at −40° C.; sp. gr. 13.5; insoluble in most solvents, including hydrochloric acid; soluble in boiling sulfuric acid and in nitric acid; boils at 358° C. For details, see U.S.P., p. 190.

For *tests for identity* and for *assay*, see U.S.P., p. 191.

Remarks.—Metallic mercury is one of the two metals recognized by the Pharmacopœia as a metal, the other being iron.

It will be noticed from the pharmacopœial description of the metal that one of the tests is that a globule of mercury rolled on paper should not leave a black mark. If it does leave a mark, it means that the mercury is contaminated with dirt, and this can be removed by straining through chamois. If there is only a small quantity of mercury to be so cleaned, it can be done by placing a plain filter in a funnel, and piercing the point of the filter with a pinhole, just large enough to permit the passage of the mercury in a very fine stream. The globules of mercury rolling down over the paper toward the pinhole will leave most of the dirt against the paper.

It must be borne in mind, however, that this process will remove only such impurities as are insoluble, and for a complete purification of the metal its distillation is advisable. To perform this is, however, a matter of difficulty, except on a large scale, and recourse is had to purification by treatment with diluted nitric acid, washing with water, drying, and expressing through chamois.

Mercury is always given medicinally in finely divided form, and of such preparations the following are official:

MASSA HYDRARGYRI—Mass of Mercury

(Mass. Hydrarg.—Blue Mass, Blue Pill)

Mass of Mercury contains not less than 32 per cent and not more than 34 per cent of Hg.

Recipe and details of manufacture see p. 329.

Remarks.—Mass of mercury is mercury extinguished (as already explained on p. 329) by oleate of mercury, honey and glycerin, the excipient (a hardener in this case) being glycyrrhiza and althea. For details of manufacture see p. 329. Mass of mercury is used as a cholagogue.

Dose.—200 mg. (3 grains).

HYDRARGYRUM CUM CRETA—Mercury with Chalk

(Hydrarg. c. Cret.—Gray Powder)

Mercury with Chalk contains not less than 37 per cent and not more than 39 per cent of Hg.

Storage.—Preserve in well-closed containers and protected from light.

Condensed Recipe.

Weigh 38 Gm. mercury and 10 Gm. honey into a stout bottle, add 2 cc. of water and shake until the mercury is extinguished (no longer visible under glass magnifying four diameters). Make a thick creamy paste of 57 Gm. prepared chalk with water in a mortar, add to it the extinguished mercury and triturate to a uniform mixture. Dry this between layers of bibulous paper and then in a dish until it weighs 100 Gm. Then powder it; bottle and keep away from the light. For details, see U.S.P.

Summarized Description.

Light gray rather damp powder, free from grit, slightly sweet taste. For details, see U.S.P., p. 192.

For *tests for identity,* for *impurities* (mercurous and mercuric oxides) and for *assay,* see U.S.P., p. 192.

Remarks.—Mercury with chalk is a finely divided form of mercury, containing from 37 to 39 per cent of metal extinguished by clarified honey, moist chalk being then added. Like all mercurial preparations made of the free metal, the extinguishing is the most tiresome, and in this special case can only be performed satisfactorily by machinery. In the finished product the mercury globules should not be seen with a glass magnifying four diameters. By bibulous paper the Pharmacopœia means an absorbent like filter- or blotting-paper.

This body is used as a cholagogue.

Dose.—250 mg. (4 grains).

UNGUENTUM HYDRARGYRI FORTE—Stronger Mercurial Ointment

Recipe.—See p. 367.

For *assay,* see U.S.P., p. 420.

Ointment of mercury contains 50 per cent of mercury, extinguished with oleate of mercury and mixed with an ointment base consisting of wool fat, white wax, and white petrolatum. (See p. 367.) Like sulfur ointment, the element is gradually absorbed by the fat, forming a mercury soap; old ointments containing as much as 4.7 per cent of mercury in saponified condition. It is used rather extensively in skin troubles, and also for destroying body vermin. For this latter purpose it is usually dispensed in diluted form.

UNGUENTUM HYDRARGYRI MITE—Mild Mercurial Ointment

This is the largely used *blue ointment* and is made by diluting the 50 per cent ointment with an ointment base consisting of white wax and white petrolatum.

In the Pharmacopœia of 1890 the 50 per cent ointment was the only one official, and its official synonym was blue ointment.

Now, the 50 per cent ointment is the one to use for obtaining the effect of mercury by inunction, the 30 per cent is much safer to use for body vermin; hence the weaker form was introduced into the eighth edition of the Pharmacopœia under the name blue ointment.

Emplastrum Hydrargyri (U.S.P. VIII), or *Mercurial Plaster*, contained 30 per cent of mercury extinguished with oleate of mercury, and then diluted with lead plaster.

Emplastrum Ammoniaci cum Hydrargyri (U.S.P. 1890).—Plaster of ammoniac and mercury, which was formerly official, contains 18 per cent of mercury, and is made by extinguishing the metal with oleate of mercury, and combining same with an acetic acid extract of ammoniac and lead plaster.

Mercurial Powder may be produced by extinguishing mercury with oil of turpentine and then triturating with lycopodium. In this way a yellow-gray powder containing 33 per cent of mercury may be obtained.

SALTS OF MERCURY

It will be recalled that, in considering iron salts, the various ferrous compounds were first discussed, and these followed by the ferric compounds. In the case of the mercury compounds, however, we can obtain a better view of the subject by comparing the two classes of salts, the "ous" and the "ic" together; hence the two chlorides will be studied together, then the two iodides, and so on.

HYDRARGYRUM AMMONIATUM—Ammoniated Mercury

(Hydrarg. Ammon.—White Precipitate)

$HgNH_2Cl$. Molecular weight, 252.09

Ammoniated Mercury contains $HgNH_2Cl$, corresponding to not less than 78 per cent and not more than 80 per cent of Hg.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White, pulverulent pieces or white, amorphous powder; earthy, then styptic, metallic taste; insoluble in water or alcohol; decomposed by prolonged washing with water, changing to a yellow basic salt; soluble in warm hydrochloric, nitric or acetic acid and in ammonium carbonate solution; soluble in solution of sodium thiosulphate with decomposition; heated below redness, dissociates; at red heat, sublimes. For details, see U.S.P., p. 191.

For *tests for identity*, for *impurities* (carbonate, mercurous salts) and for *assay*, see U.S.P., p. 191.

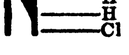
Remarks.—This compound, commonly called *white precipitate*, is made by the precipitation of the solution of mercuric chloride with ammonia water, the equation being as follows:

$$HgCl_2 + 2NH_4OH = NH_2HgCl + 2H_2O + NH_4Cl.$$

Ammoniated mercury is an interesting illustration of how a complex formula can be altered. If we add hydrochloric acid (HCl) to ammonia water (NH_4OH), we get ammonium chloride (Formula A), as already explained on p. 501.

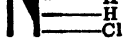
If, however, it is mercuric chloride ($HgCl_2$) that is added to ammonia water instead of hydrochloric acid, we get ammoniated mercury, NH_2-HgCl, in which two of the hydrogen atoms of the ammonium chloride are replaced by 1 atom of mercury, with the valence II, as shown in Formula B.

FORMULA A



$$N\begin{cases}-H\\-H\\-H\\-H\\-Cl\end{cases}$$

FORMULA B



$$N\begin{cases}=Hg\\-H\\-H\\-Cl\end{cases}$$

Great care must be taken in the manufacture strictly to follow the standard recipes of former Pharmacopœias. Several combinations of mercuric chloride with ammonia are known, and if the proportions of bichloride and ammonia water vary, some of these other than $HgNH_2Cl$ may be formed.

White precipitate, when treated with alcoholic solution of iodine, produces an explosion due to liberation of ammonia and nitrogen:

$$9NH_2HgCl + 6I_2 = 3NH_4Cl + 3HgCl_2 + 2NH_3 + 2N_2 + 6HgI_2.$$

Ammoniated mercury is never used internally, being always applied in the form of an ointment. Such an ointment, containing 10 per cent of ammoniated mercury, rubbed up with a base consisting of wool fat, white wax, and white petrolatum and 40 Gm. hydrous wool fat, is official under the name of *unguentum hydrargyri ammoniati.* (See p. 366.)

Sal Alembroth, $Hg(NH_4)_2Cl_4.2H_2O$, a crystalline, water-soluble salt, made by dissolving mercuric chloride and ammonium chloride in boiling water, was formerly used in medicine.

Two chlorides of mercury are recognized by the Pharmacopœia—the *mercuric chloride,* $HgCl_2$, and the *mercurous chloride,* HgCl.

HYDRARGYRI BICHLORIDUM—Mercury Bichloride

(**Hydrarg. Bichlor.**—Hydrargyri Chloridum Corrosivum U.S.P. X, Corrosive Mercuric Chloride, Corrosive Sublimate, Mercuric Chloride)

$HgCl_2$. Molecular weight, 271.52

Mercury Bichloride, when dried for twenty-four hours over sulfuric acid, contains not less than 99.5 per cent of $HgCl_2$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Heavy, colorless, rhombic crystals, or crystalline masses, or white powder; characteristic metallic taste; soluble in about 13 parts of water in about 3 parts of alcohol, in about 16 parts of glycerin and about 15.7 parts of ether; fuses at 265° C. and sublimes at about 300°. For details, see U.S.P., p. 186.

For *tests for identity,* for *impurities* (insoluble matter) and for *assay,* see U.S.P., p. 186.

This is the violent poison called *corrosive sublimate,* and is made by heating a mixture of mercuric sulfate and sodium chloride in a retort. As a result, the mercuric chloride forms and sublimes, condensing in masses, while the sodium sulfate remains in the retort, as is shown in the following equation:

$$HgSO_4 + 2NaCl = HgCl_2 + Na_2SO_4.$$

It can also be made by mixing 100 parts of mercuric sulfate, 40 parts of sodium chloride and 20 parts of 5 per cent hydrochloric acid, and after triturating to a magma and letting stand for twenty-four hours, extracting the mercuric chloride with boiling 95 per cent alcohol. There are now a number of patents for the manufacture of bichloride by the direct union of the elements, the mercury being first vaporized.

Mercuric chloride, or *bichloride of mercury,* as it is frequently called, occurs in the form of colorless, rhombic crystals or in crystalline masses. It is used internally as an alterative, and is frequently administered in combination with potassium iodide, when mercuric iodide results.

Mercuric chloride is one of the most valuable antiseptics. If it is applied to the skin in concentrated form, it is escharotic and caustic, and for this reason great care should be taken in the use of the alcoholic solution for local application.

Bichloride of mercury is a virulent corrosive poison, producing an acute type of nephritis. Antidotes are therefore usually of service only when administered shortly after the poison has been swallowed. The standard antidote is albuminous matter (white of egg or milk) forming the comparatively inert insoluble albuminate of mercury which is removed from the stomach by use of an emetic. Sodium phosphite has been deemed a useful antidote during the past twenty years and lately *Rongalite* (sodium formaldehyde sulfoxylate) has been found of value. (See p. 651.)

So widespread has been mischief produced by careless use of "bichloride tablets" that the Pharmacopœia provides *poison tablets of mercury bichloride* (large and small) (see pages 347 and 349) of distinctive shape and color.

Dose.—4 mg. (1/15 grain).

HYDRARGYRI CHLORIDUM MITE—Mild Mercurous Chloride (Hydrarg. Chlorid. Mit.—Mercurous Chloride, Calomel, Subchloride of Mercury)

HgCl. Molecular weight, 236.07

Mild Mercurous Chloride, when dried to constant weight over sulfuric acid, contains not less than 99.6 per cent of HgCl.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White, impalpable powder; yellow-white on trituration under pressure; insoluble in water, alcohol, ether and cold, diluted acids; on strong heat, volatilizes without fusion. For details, see U.S.P., p. 186.

For *tests for identity*, for *impurities* (mercuric chloride, ammoniated mercury) and for *assay*, see U.S.P., p. 186.

Remarks.—Two origins of the synonym *calomel* have been suggested. Both agree that the word is derived from the Greek word *kalos*, meaning good, and *melas*, meaning black. Some explain these words (black, good) by saying that it means that calomel was good for black bile, while others claim that it is because of the fact that calomel blackens when treated with ammonia.

As explained on p. 611, some chemists claim that calomel has the formula HgCl, while others think it is Hg_2Cl_2.

Calomel is made by a process similar to the manufacture of corrosive sublimate—*i. e.*, the mercuric sulfate is prepared by treatment of mercury with sulfuric acid, and to the mass sodium chloride is added, but before subliming there is also added an amount of mercury equal to the quantity originally used to make the mercuric sulfate. The mixture is then sublimed, as in the case of corrosive sublimate, for, be it remembered, calomel is sublimable, even as is the so-called "sublimate" ($HgCl_2$). The equation of manufacture is as follows:

$$HgSO_4 + Hg + 2NaCl = 2HgCl + Na_2SO_4.$$

The two chlorides, calomel and corrosive sublimate, afford a vivid picture of the possibly immense alteration in therapeutic or physical condition that a slight chemical difference may produce.

Between the insoluble, comparatively harmless calomel, and the soluble and virulent poison, corrosive sublimate, the only chemical difference is that the former contains more mercury than does the latter. The quantity of mercury in each is best shown by the following calculation of percentage composition of the two salts:

CORROSIVE SUBLIMATE	CALOMEL
$Hg = 1 \times 200 = 200$	$Hg_2 = 2 \times 200 = 400$
$Cl_2 = 2 \times 35.5 = \underline{71}$	$Cl_2 = 2 \times 35.5 = \underline{71}$
Molecular weight, $HgCl_2$, 271	Molecular weight, Hg_2Cl_2, 471

From this it will be seen that while corrosive sublimate is $^{200}/_{271}$, or 73.4 per cent, mercury, calomel contains $^{400}/_{471}$, or 84.9 per cent, mercury.

Since calomel and corrosive sublimate are both sublimable and are prepared by similar processes, there is always a possibility of the calomel containing traces of corrosive sublimate, and for this reason the pharmacopœial test should be applied to all samples of calomel. This test consists in shaking the sample of calomel with ether (in which it is insoluble, but which will dissolve the bichloride), evaporation of the ethereal solution, taking up residue with water, and testing water solution for bichloride either with silver nitrate or ammonium sulfide.

A simpler, though not exact, test was provided in U.S.P. 1890, namely, that calomel is totally insoluble in water, whereas, if there is any bichloride present, it will readily dissolve in water. Therefore on mixing calomel with water, the water, on being filtered, will contain bichloride, if any be present in the calomel, and can be detected by treating with ammonia and hydrogen sulfide.

Mild mercurous chloride is a valuable hepatic stimulant and alterative. In former days very large doses of calomel were given, 10 grains being considered an average dose. It has been discovered, however, that small doses frequently repeated act far better than single large doses. For this reason at present this chemical is usually administered in $^{1}/_{10}$ doses every two hours. It must be remembered that if a patient who has taken calomel is permitted to consume food containing free acids, such as lemonade, etc., that form of mercurial poisoning called salivation ensues. Hence when calomel is administered, the patient should always be warned to avoid the use of such acids until the chemical has completely acted.

A favorite method of administration of calomel is in combination with an alkali, preferably sodium bicarbonate. Large quantities of this combination are consumed in the southern States, and it might be stated that pills containing 2½ grains each of calomel and sodium bicarbonate have enjoyed considerable vogue under the name of *Dr. Stone's Little Giant Pills*. Two of these were considered a dose. Recently calomel has been employed in the treatment of syphilis, either by the intramuscular injection of an oily mixture or by rubbing in a 33 per cent calomel ointment. The latter is also used as a venereal prophylactic.

For many years, it was supposed that when calomel was triturated with sugar or with alkaline chlorides, corrosive sublimate was produced. The investigations of Schaefer (1910) indicate, however, that this is not so.

Dose.—Laxative, 150 mg. (2½ grains).

Hydrargyri Cyanidum (U.S.P. 1890).—Mercuric cyanide, $Hg(CN)_2$. This chemical is made by passing hydrocyanic acid gas into a liquid in which finely divided mercuric oxide is suspended. The hydrocyanic acid used is generally produced by treatment of potassium ferrocyanide with sulfuric acid.

Mercuric cyanide occurs in colorless prismatic crystals, turning dark on exposure to air, and is used as an alterative in syphilis, administered in doses of from 4 to 8 mg.

Two iodides of mercury are recognized by the Pharmacopœia—*mercuric iodide*, HgI_2, and *mercurous iodide*, HgI.

Hydrargyri Iodidum Rubrum (U.S.P. X; N.F. VI), or *Red Mercuric Iodide*, HgI_2, is made by the double decomposition of mercuric chloride and potassium iodide, avoiding excess of either reagent, as mercuric iodide is soluble in solutions of either chemical. This reaction takes place in many prescriptions and, as in all such prescriptions, the iodide is largely in excess, the precipitate formed invariably redissolves. A redissolved solution of the red iodide in potassium iodide is called "*Mayer's reagent*," the proportions being 13.55 Gm. mercuric chloride, 49.8 Gm. potassium iodide, and water to make 1000 cc. As cited on p. 901, this is an alkaloidal precipitant, so look out for prescriptions calling for corrosive sublimate, potassium iodide, and some tincture, or other preparation containing alkaloids, as the Mayer's reagent formed will surely precipitate the alkaloid.

The red iodide is a scarlet-red amorphous powder, insoluble in water but soluble in alcohol (93 parts), ether (86 parts), and in aqueous solutions of iodides, of mercuric chloride and of sodium thiosulfate. It is used as an alterative in syphilis and it is claimed that its bactericidal power is five to ten times greater than that of mercuric chloride.

It is now frequently administered by intravenous injection in an oleaginous base. Thus the French Codex prescribes a red iodide oil made from 0.2 Gm. of red mercuric iodide in 46 Gm. of sterilized olive oil.

As mentioned above, the physiologic effects of red mercuric iodide are obtained by prescribing a combination of potassium iodide with bichloride of mercury. Red mercuric iodide is a constituent of Donovan's solution. (See p. 212.)

Dose.—4 mg. ($\frac{1}{15}$ grain).

HYDRARGYRI IODIDUM FLAVUM—Yellow Mercurous Iodide

(Hydrarg. Iodid. Flav.—Mercurous Iodide)

HgI. Molecular weight, 327.53

Yellow Mercurous Iodide, when dried to constant weight over sulfuric acid, contains not less than 99 per cent of HgI.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Bright yellow, amorphous powder; exposed to light, dissociates into mercury and mercuric iodide and turns greenish; almost insoluble in water; insoluble in alcohol and ether; on heating, it turns orange, then red and finally volatilizes; quick heat causes partial dissociation into mercury and mercuric iodide. For details, see U.S.P., p. 187.

For *tests for identity*, for *impurities* (mercuric iodide) and for *assay*, see U.S.P., p. 187.

Remarks.—This chemical was called the *green iodide of mercury* in the Pharmacopœia of 1880. It is made by dissolving mercury in a sufficient quantity of nitric acid to form a solution of mercurous nitrate, the equation being as follows:

$$6Hg + 8HNO_3 = 6HgNO_3 + 4H_2O + N_2O_2.$$

The resulting solution of mercurous nitrate is then treated with a molecular quantity of potassium iodide, when potassium nitrate and mercurous iodide result, the latter being precipitated in the form of yellow, crystalline powder, the equation being as follows:

$$HgNO_3 + KI = HgI + KNO_3.$$

The product thus made is not the same as the green iodide of the Pharmacopœia of 1880, which was made by the direct union of mercury with iodine, triturating the two in the presence of alcohol. The equation of this reaction was supposed to be as follows:

$$Hg + I = HgI,$$

but, as a matter of fact, it partly runs as follows:

$$Hg + I_2 = HgI_2,$$

with the formation of mercuric iodide. This mercuric iodide was removed by the process of the Pharmacopœia of 1880 by washing the mixture with alcohol.

As mercurous iodide is very sensitive to light, it should be preserved in amber-colored bottles.

Mercurous iodide, like mercuric iodide, is used as an alterative, but is a much milder preparation, as is shown by the doses.

Dose.—10 mg. (1/6 grain).

While the two iodides are mercurous and mercuric respectively, both *oxides of mercury* are "ic" salts, having the formula HgO, and giving an interesting example of physical difference of two bodies that are chemically identical. Their mutual identity is proved by the fact that red oxide, when finely triturated, turns yellow, while the yellow, on heating, is converted into the red.

HYDRARGYRI OXIDUM FLAVUM—Yellow Mercuric Oxide (Hydrarg. Oxid. Flav.—Yellow Precipitate)

Yellow Mercuric Oxide, when dried to constant weight at 110° C., contains not less than 99.5 per cent of HgO.

Preserve in well-closed containers, protected from light.

Summarized Description.

Light orange-yellow amorphous, heavy, impalpable powder; somewhat metallic taste; turns somewhat dark on exposure to light; almost insoluble in water; insoluble in alcohol; soluble in diluted hydrochloric or nitric acids; on heating, it first turns red and then dissociates into oxygen and metallic mercury. For details, see U.S.P., p. 188.

For *tests for identity;* for *impurities* (red mercuric oxide) and for *assay,* see U.S.P., p. 188.

Remarks.—Yellow mercuric oxide is made by treating bichloride of mercury with the requisite amount of sodium hydroxide as shown in the following equation:

$$HgCl_2 + 2NaOH = HgO + H_2O + 2NaCl.$$

As a result, mercuric oxide is precipitated, leaving in solution sodium chloride, the last traces of which are removed from the mercuric oxide by washing with water.

Yellow mercuric oxide is used chiefly externally, and that in the form of a 1 per cent ointment (see p. 368), or of a 25 per cent solution in oleic acid. (See Oleate of Mercury, U.S.P. X, on p. 234.)

LABORATORY EXERCISE

MAKE YELLOW MERCURIC OXIDE

Recipe.—	Corrosive mercuric chloride	10 Gm.
	Sodium hydroxide	4 Gm.
	Distilled water, a sufficient quantity.	

Dissolve the corrosive mercuric chloride in 100 cc. of warm distilled water, and filter the solution. Dissolve the sodium hydroxide (which should contain at least 90 per cent of pure anhydrous sodium hydroxide) in 100 cc. of cold distilled water, and into this solution pour gradually, and with constant stirring, the solution of corrosive mercuric chloride. Allow the mixture to stand for an hour at a temperature of about 30° C., stirring frequently. Then decant the supernatant clear liquid from the precipitate, and wash the latter repeatedly by the addition and decantation of portions of distilled water, using 100 cc. of water each time. Collect the precipitate on a strainer, and continue the washing with warm distilled water until a small portion of the washings, when poured on a little mercuric chloride test solution, no longer produces a yellowish turbidity at the line of contact of the two liquids. Then allow the precipitate to drain, and dry it between sheets of bibulous paper, in a dark place, at a temperature not exceeding 30° C., and keep it in well-stoppered bottles, protected from light.

Chemical Explanation.—When solutions of mercuric chloride and of sodium hydroxide are combined, yellow mercuric oxide is precipitated by the following reaction:

Mercuric chloride	plus	Sodium hydroxide	give	Mercuric oxide	plus	Water	plus	Sodium chloride.
$HgCl_2$	+	NaOH	=		+		+	

Complete this equation.

Calculations.—Work out molecular weights of mercuric chloride, sodium hydroxide, and mercuric oxide (HgO). From these figures work out the following examples:

1. How many grams of mercuric oxide can be made from 271 Gm. mercuric chloride?
2. How many grams of mercuric oxide can be made from 10 Gm. mercuric chloride?
3. How many grams of sodium hydroxide (100 per cent) will combine with 271 Gm. mercuric chloride?
4. How many grams of sodium hydroxide (85 per cent) will combine with 271 Gm. mercuric chloride?
5. How many grams of sodium hydroxide (85 per cent) will combine with 10 Gm. mercuric chloride?

Compare with figures given above, and weigh your finished mercuric oxide to see if it agrees with the theoretic yield.

In the recipe given above, which was that of U.S.P. VIII the excess of sodium hydroxide is to insure complete precipitation of the mercury, the surplus soda being washed out of the precipitate with water.

Remarks on Process.—*Dissolve the mercuric chloride* in Erlenmeyer flask and filter into an 8-ounce wide-mouthed bottle.

Dissolve the sodium hydroxide in pint flask, and into this pour the mercuric chloride solution.

Wash the precipitate by decantation as far as possible, and finally *throw precipitate on plain filter*, instead of on strainer, as U.S.P. VIII directed. Were we making the pharmacopœial quantity (ten times our present amount), a strainer would be indicated, but with the small amount we have, a plain filter will suffice.

Wash until washings no longer respond with mercuric chloride test solution—that is, until free from sodium hydroxide. If the hydroxide is present in water, a yellow precipitate (HgO) is produced with mercuric chloride solution.

In testing for sodium hydroxide place about 1 inch of the mercuric solution in test tube and pour thereon very gently, along tilted test tube, the washings, so as to permit the washings to float on the surface of the mercuric chloride solution, thus forming two layers; where the two layers join—"the point of contact"—the yellow color appears.

Hydrargyri Oxidum Rubrum (N.F. VI) or *Red Mercuric Oxide* is also called *"red precipitate."* It is, however, no longer prepared by precipitation, the name being a souvenir of alchemistic days, when it was made by "upward precipitation," being formed in mercury kept near its boiling-point for weeks at a time.

It is now made by treating mercury with nitric acid (equation *a*) and heating the resulting mercuric nitrate to redness (equation *b*):

$$(a)\quad 3Hg + 8HNO_3 = 3Hg(NO_3)_2 + 4H_2O + N_2O_2.$$
$$(b)\quad 2Hg(NO_3)_2 + \text{heat} = 2HgO + 2N_2O_4 + O_2.$$

It will be seen from the above equations that the nitrate is dissociated into mercuric oxide, N_2O_4, and oxygen, and experience has shown that the two gases are capable of converting into mercuric oxide an amount of mercury equal to the amount of the nitrate used originally.

Red mercuric oxide is a heavy red powder, turning yellow on trituration. It is used almost entirely externally, and that chiefly in the form of an ointment for granulated eyelids.

The National Formulary recognizes a 10 per cent ointment (p. 372).

Hydrargyri Subsulfas Flavus (U.S.P. 1890).—The formerly official *yellow mercuric subsulfate* is a basic salt. As already explained on p. 570 "sub"-salt is a combination of a metallic salt with its oxide, and in the case under consideration we find the relationship clearly shown in the symbolic formula, $HgSO_4(HgO)_2$. It is called *Turpeth mineral*, on account of its resemblance to the powdered turpeth root, the root of *Ipomœa turpethum*, which was formerly used in medicine.

Turpeth mineral is made by treating mercury with a mixture of sulfuric acid and nitric acids, whereby mercuric sulfate is formed, as shown in the following equation:

$$3Hg + 3H_2SO_4 + 2HNO_3 = 3HgSO_4 + 4H_2O + N_2O_2.$$

The white mercuric sulfate is then heated with a large quantity of water, whereby it is converted into the yellow mercuric subsulfate, as shown in the following equation:

$$3HgSO_4 + 2H_2O = HgSO_4 2HgO + 2H_2SO_4.$$

Turpeth mineral is an alterative, possessing, however, such irritating qualities as to render its general use unsafe. It is administered in doses of from 16 to 30 mg.

Mercuric Nitrate, $Hg(NO_3)_2$, is not recognized by the Pharmacopœia as a chemical itself, but two preparations containing this chemical have extensive use.

Liquor Hydrargyri Nitratis (U.S.P. VIII; N.F. IV), or *Solution of Mercuric Nitrate*, is made by dissolving 40 Gm. of mercuric oxide in a mixture of 45 Gm. of nitric acid

and 15 Gm. of distilled water. It is a very heavy fluid, weighing more than twice as much as water (sp. gr. 2.086).

Solution of mercuric nitrate is used entirely locally as a corrosive in syphilitic sores.

Unguentum Hydrargyri Nitratis (N.F. VI), or *Citrine Ointment*, is made by heating lard to 45° C., adding thereto nitric acid. When the nitric acid is added to the heated lard, a rather violent chemical action takes place, with the conversion of the oleate of glyceryl, which is the chief constituent of the lard, into elaidin. (See p. 727.)

Mercury is dissolved in a second portion of nitric acid, forming mercuric nitrate, and it might be said in passing that when mercury is dissolved in nitric acid we get mercurous or mercuric nitrate, according to the relative proportions of mercury and nitric acid employed:

$$3Hg + 8HNO_3 = 4H_2O + N_2O_2 + 3Hg(NO_3)_2 \text{ (Mercu}\textit{ric}\text{ nitrate).}$$
$$6Hg + 8HNO_3 = 4H_2O + N_2O_2 + 6HgNO_3 \text{ (Mercur}\textit{ous}\text{ nitrate).}$$

That the proportions of mercury and nitric acid used in the National Formulary recipe yield mercuric nitrate is shown by the molecular weight calculations relating to citrine ointment found below.

It may be well to sum up here the effect of various acids on metals.

Hydrochloric and *other haloid acids* and *diluted sulfuric acid* give, with most metals the appropriate salt, *with the evolution of hydrogen.* Example:

$$Zn + H_2SO_4 = ZnSO_4 + H_2.$$

Nitric acid, either concentrated or diluted, and *concentrated sulfuric acid*, give with metals the appropriate salt, with the *evolution of N_2O_2* or *N_2O_4*, in the case of nitric acid, and of SO_2 in the case of sulfuric acid. Examples of nitric acid are given just above. Of concentrated sulfuric acid, see Copper Sulfate (p. 595).

Citrine ointment (from *citrus*, the lemon) has, as the name suggests, a bright yellow color when freshly prepared; on standing, however, it assumes a brown tint. The manufacture of this compound is one calling for considerable skill in order to obtain a product of exactly the right color and consistence and of the same quality. The quality of lard oil found in the market was so variable that, in the eighth revision of the Pharmacopœia, the lard oil of U.S.P. 1890 was replaced by the more reliable lard.

Citrine ointment is a valuable remedy for certain forms of skin trouble, such as tetter and ringworm.

LABORATORY EXERCISE

MAKE OINTMENT OF MERCURIC NITRATE

Recipe.—	Mercury	7.0 Gm.
	Nitric acid	17.5 Gm.
	Lard, free from water	76.0 Gm.
	To make about	100 Gm.

Heat the lard in a capacious glass or porcelain vessel to a temperature of 105° C., then withdraw the heat, and gradually add 7 Gm. of the nitric acid. When the reaction moderates, reapply the heat until effervescence ceases, and allow the mixture to cool to about 40° C. Having dissolved the mercury in the remainder of the nitric acid, using sufficient heat to prevent the solution from crystallizing, add this solution to the lard mixture. When the mass begins to congeal, stir it thoroughly with a wooden spatula until it is of a bright citrine color. Contact with metallic utensils should be avoided.

Chemical Explanation.—In this preparation two distinct reactions occur: In the first place, mercury dissolves in nitric acid to make mercuric nitrate by either of the following equations:

$$Hg + 4HNO_3 = Hg(NO_3)_2 + N_2O_4 + H_2O.$$
$$3Hg + 8NHO_3 = Hg(NO_3)_2 + N_2O_2 + H_2O.$$

Complete these equations.

Then the white lard is converted into the lemon yellow solid elaidin when the nitric acid is added to it.

Elaidin has the same empiric formula as has the olein of the oil, and since the chemistry of the change is complicated (see p. 727), no molecular weight calculation will be made.

Calculations.—As just mentioned, no calculation can be made on the conversion of olein of the lard into elaidin, nor is the amount of nitric acid used in dissolving the mercury in accord with molecular proportions; hence the amount will not be determined.

Remarks on Process.—The foregoing recipe is similar to but not identical with that of N.F. VI. The Formulary directs that the heat of reaction be 45° C. The writer's experience has been that a temperature of at least 100° C. is essential to a successful reaction. The secret of making a satisfactory preparation is largely the proper control of the temperature as explained below.

Put lard in pint evaporating dish and heat to 105° C. on wire gauze.

A water bath will not do, as the lard must be heated to 105° C. in order to get reaction started.

Add the nitric acid gradually, not allowing heat to get too intense. If reaction has gone nicely, an orange-colored liquid results; if overheated, the lard turns chocolate brown.

Reapply heat until effervescence ceases. This must be done, cautiously, else the mass will turn dark. It must be heated enough, or else the finished product will "work," frothing out of container.

Dissolve the mercury in nitric acid in Erlenmeyer flask. Better start it before treating the lard with nitric acid.

If mercuric nitrate solution crystallizes, warm it before mixing with the elaidin mixture.

Use glass rod during the elaidin reaction, and employ a wooden paddle for mixing in the mercuric nitrate solution.

HYDRARGYRI SALICYLAS—Mercuric Salicylate

(Hydrarg. Salicyl.)

$HgC_7H_4O_3$. Molecular weight, 336.64

Mercuric Salicylate is a compound of mercury and salicylic acid containing not less than 54 per cent and not more than 59.5 per cent of Hg.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White, slightly yellowish or slightly pinkish powder; nearly insoluble in water or alcohol; soluble in warm solutions of alkali halides, alkali hydroxides and alkali carbonates. For details, see U.S.P., p. 189.

For *tests for identity,* for *impurities* (free salicylic acid, foreign mercury compounds) and for *assay,* see U.S.P., p. 189.

Remarks.—This official is prepared by heating a freshly precipitated yellow mercuric oxide with the molecular quantity of salicylic acid and with a little water until a perfectly white mixture results. It is a white powder, insoluble in water and is used as an antiseptic and antisyphilitic. For the latter purpose it is usually injected in the form of a suspension in oils.

Dose.—Intramuscular: 60 mg. (1 grain) twice a week.

Mercuric Sulfide (U.S.P. 1880) is the artificial *cinnabar,* and is made by the sublimation of the black sulfide. The latter, formerly called *Æthiops mineral,* has been mentioned as the precipitate formed by passing hydrogen sulfide through solutions of mercuric salts, but is made commercially by fusing sulfur with mercury. Both sulfides have the formula HgS, the only difference being that the red is crystalline, while the black is amorphous. Cinnabar is practically never used internally.

SILVER

Symbol, Ag. Atomic weight, approximately 108

Silver occurs occasionally in the form of the pure metal, but its most abundant ores are silver sulfide, which is called *silver glance,* and the chloride, or *horn silver.* A very large quantity of silver is obtained from the silver-bearing galena. (See p. 604.)

Silver is one of the ancient metals, reference to it being found in the earliest writings. Silver salts were also known to the ancient Egyptians, since some mummy clothes are marked with indelible (silver nitrate) ink. The Latin word *argentum* is derived from the Greek for silver, *arguros,* which in turn derived from the Greek word *argos,* meaning shining.

The *metallurgy* of silver is interesting and important, and can be roughly divided into four groups. The first include the wet extraction process. In one of these the sulfides (galena or silver glance) is roasted with sodium chloride, thus changing the silver to silver chloride. The roasted mass is then ground, placed in appropriate hoppers, percolated with an aqueous solution of sodium thiosulfate, in which the chloride is soluble; calcium sulfide is added to the percolate, causing the precipitation of silver sulfide. The pure silver is obtained by roasting the sulfide, while the thiosulfate is recovered from the filtrate and used again.

Another method is by carefully roasting the ores, whereby the silver sulfide contained therein is converted into sulfate, and this is extracted by percolation of the roasted mass with water. Metallic silver is separated from the percolate by use of metallic copper.

The second group of processes are those where amalgamation is employed. In these the ore is roasted with salt, changing the silver sulfide found therein to silver chloride. This is reduced with iron or with copper sulfate to metallic silver, which forms an amalgam with mercury. This amalgam is separated from the solid matter and is heated in a retort, when the mercury distils leaving a residue of metallic silver.

The third group of processes are those where *cupellation* is employed, and is applied to ores containing lead and silver. Such ores are roasted in furnaces with free exposure to air, the result being the liberation of metallic silver and the conversion of lead into litharge, which is skimmed off. Lastly, *electrolytic separation* of silver from copper-bearing ores is now being employed.

Silver is a brilliant white, malleable, ductile metal, about 10.5 times heavier than water, soluble in nitric acid, and but sparingly soluble in sulfuric acid. While in the molten condition it has a great affinity for oxygen, absorbing no less than twenty-two times its volume of that gas. On cooling, it parts with all its oxygen: frequently with explosive violence. This property makes the melting of silver a process requiring considerable care. The silver used in coins (sterling silver) consists of 92.5 per cent of silver and 7.5 per cent of copper, it being so admixed because pure silver is too soft to be used alone.

Silver is called a "noble metal," partly because it costs more than the common metals already considered, and chiefly because it withstands the oxidizing action of the atmosphere. This property it shares with gold and platinum and also in a lesser degree with aluminum and nickel.

The *tests* for silver are as follows:

Hydrochloric acid produces a precipitate of white silver chloride, insoluble in nitric acid, but soluble in ammonia water. Hydrogen sulfide or ammonium sulfide produces a black precipitate of silver sulfide, while potassium hydroxide precipitates silver from its soluble salts in the form of a brown silver oxide.

The oxides of silver which are known are Ag_2O, Ag_2O_2, and Ag_4O. Of these, the first is the only one of sufficient importance to merit more than passing notice. It was recognized by former Pharmacopœias, and in constitution is analogous to sodium oxide, Na_2O, exhibiting silver with valence I.

The official salts of silver are:

Silver nitrate. At least 99.8 per cent absolute $AgNO_3$.
Toughened silver nitrate. At least 94.5 per cent absolute $AgNO_3$.
Strong silver protein. 7.5 to 8.5 per cent Ag.
Mild silver protein. 19 to 25 per cent Ag.

In considering these, the nitrate will be the first taken up, since from it all the other official silver compounds are made.

ARGENTI NITRAS—Silver Nitrate
(Arg. Nitras)

$AgNO_3$. Molecular weight, 169.89

Silver Nitrate, when powdered and dried to constant weight in the dark over sulfuric acid, contains not less than 99.8 per cent of $AgNO_3$.

Storage.—Preserve in glass-stoppered bottles, and protected from light.

Summarized Description.

Colorless, tabular, rhombic crystals; turns gray or grayish black on exposure to light; bitter, metallic taste; very caustic; soluble in 0.4 part of water and in 24 parts of alcohol; slightly soluble in ether; on heating to 200° C. it melts; at higher heat it dissociates. For details, see U.S.P., p. 69.

For *tests for identity*, for *impurities* (copper) and for *assay*, see U.S.P., p. 69.

Remarks.—This salt is made by dissolving silver coin in nitric acid, evaporating the solution to dryness, fusing, adding water to the fused mass, and filtering the silver nitrate solution from the copper oxide residue.

Silver coin is far more accessible than pure silver, hence is employed in making the nitrate. But in this process not only does the silver unite with the acid to form the nitrate, but, likewise, the copper forms copper nitrate, and, of course, a silver nitrate containing copper nitrate would not answer. The copper is removed in an ingenious way. Silver nitrate melts unchanged at 200° C., and at that temperature copper nitrate is decomposed into the gaseous oxides of nitrogen and into copper oxide, which remains behind, an insoluble mass. The fused mass is treated with water, in which the silver nitrate dissolves, leaving copper oxide behind.

Obviously silver nitrate may be prepared from pure (99.9 per cent) silver and at present this method is being used commercially in place of the more cumbersome process just described.

The time-honored conclusion that pure silver nitrate darkens on exposure to light is not indicated by the research of Arny and his coworkers who find that when the nitrate does darken it is due to the presence of hydrochloric acid. It is the silver chloride that darkens, not the nitrate. Chemically pure silver nitrate sealed in an ampul does not darken even when exposed to sunshine. Both the chloride and the bromide are very sensitive to light. The blackening of silver bromide by the influence of light constitutes the foundation of the art of photography.

Stains of silver nitrate on the skin can be removed by painting with tincture of iodine (thus producing silver iodide) and then removing the latter stain with a solution of sodium thiosulfate or ammonia water.

Silver nitrate is a valuable remedy, used both externally and internally. It is used internally in cases of gastritis and diarrhea in small doses, while large quantities act as a caustic and escharotic. If given in an overdose, the antidote is sodium chloride, which produces a mild and comparatively inert silver chloride. Externally, it is of considerable value as a caustic, but the application should be made with great care. For external use two other forms of silver nitrate are employed, the fused and the diluted.

Dose.—10 mg. (1/6 grain).

ARGENTI NITRAS INDURATUS—Toughened Silver Nitrate
(Arg. Nitras Indur.—Argenti Nitras Fusus U.S.P. X, Molded Silver Nitrate, Lunar Caustic, Fused Silver Nitrate)

Toughened Silver Nitrate contains not less than 94.5 per cent of $AgNO_3$.

***Storage.*—Preserve in glass-stoppered bottles, in a cool place and protected from light.**

Condensed Recipe. (U.S.P. IX.)

Add 4 Gm. hydrochloric acid to 100 Gm. silver nitrate, melt in a porcelain dish and pour into suitable molds.

Summarized Description.

White, hard solid, usually in the form of pencils or cones; fibrous fracture; turns gray or grayish black on exposure to light; bitter, strongly metallic taste; very caustic; soluble (except the silver chloride present) in 0.4 part of water and 24 parts of alcohol; slightly soluble in ether. For details, see U.S.P., p. 70.

For *tests for identity*, for *impurities*, see silver nitrate.

Remarks.—Fused silver nitrate is made by melting silver nitrate in a porcelain capsule, adding thereto 4 per cent of hydrochloric acid, and pouring the melted mixture into suitable molds. The hydrochloric acid used in this case is for the purpose of rendering the silver nitrate tougher and less brittle by the formation of a small quantity of silver chloride. Hughes points out that it is better to replace the hydrochloric acid with sodium chloride.

The melted silver nitrate is called *lunar caustic* (from *luna*, Latin for moon), and the application of this case is an interesting relic of alchemistic nomenclature. The alchemists, the forerunners of the modern chemists, assigned to the commoner metals the names of the heavenly bodies. Thus, gold was the sun; silver, the moon (Luna); iron was Mars; copper was Venus; lead was Saturn; while quicksilver was, as it is now, Mercury. In old names that are still used—like "boule de Mars" (iron and potassium tartrate), "*acetum Saturni*" (solution of lead subacetate), and "lunar caustic"—we find these terms still existing.

Molded silver nitrate is also called *lapis infernalis* (*stone of Hell*).

Argenti Nitras Mitigatus (U.S.P. VIII), or *Mitigated Caustic*, is made by melting together 30 parts of silver nitrate and 60 parts of potassium nitrate. As silver nitrate is a very powerful caustic, it is sometimes found wise to apply it in this diluted form.

Argenti Cyanidum (U.S.P. VIII), or *Silver Cyanide*, AgCN, is made by passing hydrocyanic acid gas through a solution of silver nitrate. It can also be made by treating potassium cyanide with silver nitrate.

It affords a simple method of extemporaneous preparation of diluted hydrocyanic acid. This acid is quite unstable, and should be fresh when dispensed. This rule is easily followed if the acid is made from silver cyanide and hydrochloric acid, the hydrocyanic acid that is formed remains in solution, while the silver chloride separates out and can be filtered off.

Argenti Iodidum (U.S.P. 1890), or *Silver Iodide*, is made by combining a solution of potassium iodide and silver nitrate and collecting the precipitated silver iodide, as shown in the following equation:

$$KI + AgNO_3 = KNO_3 + AgI.$$

This is a heavy yellow powder, and is used as an alterative in syphilis, in doses of 0.03 to 0.12 Gm. (½ to 4 grains.)

There is some demand for silver iodide in emulsified form and this can be prepared by dissolving the molecular quantity of potassium iodide in a 0.3 of 1 per cent solution of gelatin and adding to this, little by little, the proper quantity of silver nitrate in aqueous solution. The proportional amounts are obviously 165 parts of potassium iodide to 169 parts of silver nitrate. If the amount of potassium iodide is increased, a colloidal solution of silver iodide is obtained.

Argenti Oxidum (U.S.P. IX) or *Silver Oxide*, Ag_2O, is prepared by precipitating silver nitrate solution with potassium hydroxide solution, as shown in the following equation:

$$2AgNO_3 + 2KOH = Ag_2O + 2KNO_3 + H_2O.$$

Silver oxide is a dark brownish-black powder that is liable to explode when triturated with readily oxidizable or combustible substances or when treated with ammonia. It must therefore be handled very carefully.

The only safe way of making pills of silver oxide is to use petroleum mass (kaolin and petrolatum) as excipient. (See p. 332.) Also beware of bringing it in contact with ammonia, for the two will form the dangerous explosive, fulminating silver.

Silver oxide is one of the most valuable compounds of silver for internal use, it being far less caustic than any of the other silver compounds. *Dose.*—60 mg. (1 grain).

Colloidal silver preparations have been extensively used of late in place of silver nitrate and silver oxide. These are based on the remarkable fact that if a soluble silver salt is reduced under proper conditions, the metallic silver thus produced is water soluble, due, it is claimed, to the fact that the metal is in such finely divided form (slightly above molecular condition) that a colloidal solution (p. 408) obtains. Colloidal silver can be prepared by adding to 10 per cent silver nitrate solution 30 per cent ferrous sulfate solution, 40 per cent sodium citrate solution and 10 per cent sodium carbonate solution. A lilac precipitate containing 97 per cent of silver results and this after washing free from impurities with ammonia citrate solution is soluble in water or 10 per cent sodium chloride solution.

Commercial products are usually prepared containing proteids, such compounds having been found to yield more stable solutions.

There has been some discussion as to the condition of the silver in these commercial colloidal preparations. Giesy and Smith after a potentiometric (p. 1034) study of them incline to the belief that strong silver protein is a mixture of colloidal silver oxide and of silver protein, while in mild silver protein 11 to 14 per cent of its total silver content is ionizable and the balance is metallic silver in colloidal form.

U.S.P. XI recognizes two typical forms of these silver preparations, *strong silver protein* and *mild silver protein.*

ARGENTUM PROTEINICUM FORTE—Strong Protein Silver

(**Arg. Prot. Fort.**—Argento-Proteinum Forte U.S.P. X, Strong Silver Protein, Strong Protargin)

A compound of silver and protein, containing not less than 7.5 and not more than 8.5 per cent of Ag.

Caution.—Solutions of strong protein silver should be freshly prepared and should be dispensed in amber-colored bottles.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Brown, odorless powder; somewhat hygroscopic; freely soluble in water; almost insoluble in alcohol and ether. For details, see U.S.P., p. 70.

For *tests for identity,* for *impurities* (mild silver protein) and for *assay,* see U.S.P., p. 70.

Remarks.—This preparation is supposed to cover the *protargol* type of silver preparations. These are supposed to be made by precipitating a peptone solution with silver nitrate or with moist silver oxide; dissolving the silver peptonate in an excess of protalbumose and then drying in vacuo.

It is used in 0.1 to 2 per cent aqueous solution as an antiseptic and germicide for infected mucous membranes. The solution should be freshly prepared.

Rosenthaler finds that the addition of 2 parts of urea to 1 part of protargol renders the silver compound more readily soluble.

Samaan finds that while colloidal silver preparations are less efficient as disinfectants than is ionic silver (*e. g.*, silver nitrate) a 1 : 5000 solution of colloidal silver is a stronger disinfectant than phenol solution, 1 : 250. Moreover, the colloidal silver solutions are much less irritating, and are much safer to use than is silver nitrate solution.

ARGENTUM PROTEINICUM MITE—Mild Protein Silver

(Arg. Prot. Mit.—Argento-Proteinum Mite U.S.P. X, Mild Silver Protein, Mild Protargin)

Silver rendered colloidal by the presence of, or combination with, protein. It contains not less than 19 per cent and not more than 25 per cent of Ag.

Caution.—Solutions of mild protein silver should be freshly prepared and should be dispensed in amber-colored bottles.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Dark brown, shining, odorless scales or granules; somewhat hygroscopic; freely soluble in water; almost insoluble in alcohol and ether. For details, see U.S.P., p. 71.

For *tests for identity,* for *impurities* (strong silver protein) and for *assay,* see U.S.P., p. 71.

Remarks.—The preparation covers the *argyrol* type of silver preparations. These are said to be made by denaturing serum albumin by electrolysis, combining the suspended protein with moist silver oxide by heating under pressure and then evaporating in vacuo.

It is used as an antiseptic and germicide in 5 to 50 per cent solution, which acts as a mucilaginous demulcent and protective. Like the strong silver protein, the mild form must be used only in freshly made solutions. It is quite interesting to note that the words "strong" and "mild" used in connection with these two silver preparations refer to therapeutic activity and not to silver content; the one with the higher silver content exhibiting milder action.

A third group of colloidal silver preparations are those of the *collargol* type. These contain as much as 78 per cent of colloidal silver stabilized with egg albumen.

BIBLIOGRAPHY

Lead.—(History) Lippmann, Zt. angew. Ch., 18, 1905, 1213; Hackh. A.J.P., 90, 1918, 491; Louis, Jl. Soc. Ch. Ind., 42, 1923, 252 and 286; Dyson, Ph. Jl., 125, 1930, 286, 302, 386 and 406. (Production) Cuno, Jl. Ind. Eng. Ch., 23, 1931, 108. (Metallurgy) Hofman, Eng. Min. Jl., 99, 1915, 89; Stoddart, Ch. News, 42, 1880, 281. (Solder) Feldhaus, Ch. Zt., 34, 1910, 1133. (Corrosion of pipes) Heap, Jl. Soc. Ch. Ind., 32, 1913, 771, 811 and 847.

Litharge.—(History) Bailey, Pharm. Era, 61, 1925, 656.

Red Lead.—Phillips, A.J.P., 6, 1834, 162; Dumas, A.J.P., 4, 1832, 349 and 13, 1842, 169; Milbauer, C.A., 8, 1914, 2955; West, *ibid.*, 8, 1914, 3125; Bailey (see above).

Lead Suboxide.—Van Arkel, C.A., 19, 1925, 3440; Ferrari, C.A., 21, 1927, 542.

Lead Acetate.—Bell, Ph. Jl., 10, 1850, 300.

Goulard's Extract.—(History) Wootton, 1, 1910, 265; X-rayser II, Ch. and Dr., 90, 1918, 49; Cooper, Spatula, 27, 1920; Raubenheimer, Jl. A.Ph.A., 18, 1929, 270. (Composition) Morton, Quart. Jl. Ph., 5, 1932, 414. (Manufacture) Berry, Jl. Soc. Ch. Ind., 49, 1930, 1045B. (Incompatibility) Tilden, Ph. Jl., [3], 2, 1871, 123; Gibson and Matthews, C.A., 22, 1928, 1965.

Goulard's Cerate.—(History) Wootton, 1, 1910, 265.

White Lead.—(History) Bailey, Pharm. Era, 61, 1925, 656. (Structure) Hochstetter, Jl. de ph. et ch., 2, 1842, 428; Falk, Ch. Zt., 34, 1910, 937; Sacher, Ch. Zt., 34, 1910, 737; Hof, Ch. Zt., 34, 1910, 784; Owens, C.A., 8, 1914, 2625; Euston, Jl. Ind. Eng. Ch., 6, 1914, 202; Sauer and Zipfel, C.A., 26, 1932, 2068. (Manufacture) Pelouze, Jl. de ph. et ch., 1, 1842, 443; Booth, A.J.P., 14, 1842, 66; Shaw, Jl. Soc. Ch. Ind., 43, 1924, 184B.

Lead Iodide.—(History and manufacture) Denot, Jl. de ph., 20, 1834, 1. (Manufacture and properties) Duhamel, A.J.P., 6, 1834, 108.

Lead Nitrate.—Procter, A.J.P., 19, 1847, 269.

Mercury.—(History) Lippmann, Zt. angew. Ch., 21, 1908, 1781; Hackh, A.J.P., 90, 1918, 492; Raubenheimer, Jl. A.Ph.A., 7, 1918, 445; Van Derventer, C.A., 15, 1921, 780; Kremers, Jl. A.Ph.A., 18, 1929, 398. (History and source) Anon., Ph. Jl., 14, 1855, 373; Anon., Ch. and Dr., 34, 1889, 569; Dyson, Ph. Jl., 122, 1929, 466, 516 and 568. (Sources) Goldschmidt, C.A., 24, 1930, 4246; Schuette, C.A., 24, 1930, 4485. (Production) Anon., Jl. Soc. Ch. Ind., 47, 1928, 701; Anon., Jl. Frank. Inst., 208, 1929,

122; Anon., Jl. Ind. Eng. Ch., News Ed., 9, 1931, 189; Anon., Jl. Ind. Eng. Ch., 24, 1932, 538. (Metallurgy) Weiskopf, Zt. angew. Ch., 14, 1901, 429; Anon., Yearbook A.Ph.A., 7, 1918, 375; Innes, C.A., 12, 1918, 1748; Dyson, Pharm. Era, 60, 1925, 647; Duschak and Schuette, Jl. Frank. Inst., 200, 1925, 544; Schuette, Bur. Mines Bull., 335, 1931, 1–168. (Purifying) Dent., Jl. Soc. Ch. Ind., 47, 1928, 618; Feldhoff, C.A., 24, 1930, 1181. (Properties) Anon., Ch. News, 118, 1919, 129; Scheel and Blankenstein, Jl. Frank. Inst., 199, 1925, 684; Sunier and Weiner, Jl. Am. Ch. Soc., 53, 1931, 1714. (Dental amalgams) Cattell, Dental Cosmos, 64, 1922, 855; Sellner, Jl. Ind. Eng. Ch. News Ed., 4, Sept. 10, 1926, 8; Stock, Jl. Soc. Ch. Ind., 47, 1928, 676B; Hertz, C.A., 23, 1929, 3019; Gibson, Jl. Soc. Ch. Ind., 51, 1932, 452.

Black Wash and Yellow Wash.—Jean Fernal (16th cent.), Wootton, 1, 1910, 414.

Mercury with Chalk.—(History and manufacture) Bell, Ph. Jl., 1, 1841, 194; Hamilton, A.J.P., 14, 1842, 46 and 53. (Manufacture) Coxe, A.J.P., 22, 1850, 316; Boa, Ph. Jl., 104, 1920, 200; Dott, Pharm. Era, 53, 1920, 168; Golse, C.A., 24, 1930, 2547; Vitte, Jl. Soc. Ch. Ind., 25, 1931, 5504.

Blue Mass.—(History) De Bayro (1537), Wootton, 1, 1910, 412.

Blue Ointment.—(History) Mesuë (10th–11th cent.), Wootton, 1, 1910, 409. (Composition) Menschel, Jl. Soc. Ch. Ind., 42, 1923, 627A. (Preparation) Holdermann, C.A., 23, 1929, 5004; Franklin, Ph. Jl., 121, 1928, 85.

Mercurial Powder.—Unna, Ch. and Dr., 86, 115, 744.

Ammoniated Mercury.—(History and manufacture) Kane, A.J.P., 9, 1837, 252; Kolthoff, Ph. Week., 55, 1918, 208.

Corrosive Mercuric Chloride.—(History) Geber, Wootton, 1, 1910, 105. (Manufacture) Gleck, A.J.P., 39, 1867, 416; Rupp and Klee, A.Ph.A., 58, 1910, 276; Trutzer, C.A., 8, 1914, 79 and 974. (Action) Anon., Dr. Cr., 57, 1913, 317. (Antidotes) Hall, Dr. Circ., 58, 1914, 719; Carter, Dr. Circ., 58, 1914, 345; Fantus, Jl. A.M.A., 67, 1916, 1184; Vogel and Scoville, Bull. Pharm., 32, 1918, 216; Zeigler, Jl. Sub. Clin. Med., Jan., 1925; Mitchell, C.A., 18, 1924, 2296; Haskell and Forbes, C.A., 23, 1929, 3023; Rosenthal, A.J.P., 106, 1934, 5. (Tablets) Raubenheimer, Jl. A.Ph.A., 3, 1914.

Mild Mercurous Chloride.—(History and etymology) Wootton, 1, 1910, 418. (Manufacture) Soubeiran, A.J.P., 15, 1844, 89; Calvert, A.J.P., 15, 1844, 931; Duret, Ph. Jl., 103, 1919, 142. (Properties) Crollius (16th cent.), Wootton, 1, 1910, 418; LaWall and Harrisson Jl. A.Ph.A., 24, 1935, 97. (Structure) Smith and Menzies, Zt. phys. Ch., 76, 1911, 713. (Decomposition) Schaefer, Merck's Rep., 19, 1910, 123 and 153; Rebald, A.J.P., 98, 1926, 429; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1154.

Calomel Injection.—Boileau, Am. Dr., 56, 1910, 108.

Calomel Ointment.—Duret, Ph. Week., 56, 1919, 1399; Cole and Littman, Ph. Jl., 104, 1920, 46.

Red Mercuric Iodide.—(Manufacture) Boullay, Jl. de ph., 13, 1827, 435; Duhamel, A.J.P., 6, 1834, 106. (Physical properties) Tamman, Ph. Jl., 105, 1920, 8; Pélabon, C.A., 18, 1924, 2296. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1154. (Antiseptic action) Stassano and Gompel, C.A., 8, 1914, 3573; Hamilton, Jl. A.Ph.A., 9, 1920, 497. (Oleaginous solution) Dunning, A.Ph.A., 58, 1910, 1123.

Mayer's Reagent.—Mayer, A.Ph.A., 10, 1862, 239; Travell, Jl. A.Ph.A., 23, 1934, 689.

Yellow Mercurous Iodide.—(Manufacture) Boullay, Jl. de ph., 13, 1827, 435; Berthemot, Jl. de ph., 17, 1831, 457; Duhamel, A.J.P., 6, 1834, 105; Agrestini, C.A., 25, 1931, 4481. (Decomposition by light) Leffman, Jl. Frank. Inst., 195, 1923, 349; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1154.

Mercuric Oxides.—(Composition) Schoch, Am. Ch. Jl., 29, 1903, 319.

Red Mercuric Oxide.—(History) Boyle (17th cent.), Wootton, 1, 1910, 417; Holmyard, Jl. Soc. Ch. Ind., 43, 1924, 659. (Manufacture and properties) Schoch, Am. Ch. Jl., 29, 1903, 320; Zachariasen, C.A., 21, 1927, 3777; Anon., Ch. News, 121, 1920, 312. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1154.

Yellow Mercuric Oxide.—(Manufacture and properties) Schoch, see above. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1154.

Turpeth Mineral.—(History) Crollius (16th cent.), Wootton, 1, 1910, 417. (Composition) Spring. A., 199, 1879, 125. (Manufacture) Hildebrandt (1793), Gmelin-Kraut, 5^2, 1912, 599; Cox, Zt. anorg. Ch., 40, 1904, 165.

Citrine Ointment.—(History) X-rayser, Ch. and Dr., 84, 1914, 563. (Manufacture) Rother, A.J.P., 42, 1870, 417; Reichardt, A.Ph.A., 32, 1884, 57; Duncan, Ph. Jl., 119, 1927, 694.

Cinnabar and Vermilion.—Anon., Ch. News, 50, 1884, 77; Bailey, Pharm. Era, 61, 1925, 655.

Mercuric Salicylate.—Boedecker and Wunstorf, Arch. d. Pharm., 263, 1925, 430; Rupp, *ibid.*, 266, 1928, 504; Brenans and Rapilly, C.A., 26, 1932, 123.

Silver.—(History) Lippmann, Ch. Zt., 37, 1913, 934 and 963; Hackh, A.J.P., 90, 1918, 489; Dyson, Ph. Jl., 123, 1929, 117. (Metallurgy) Eggleston, J. B., 2, 1884, 1702; Bradford, Ch. Cent., 2, 1902, 1348; Dyes, Zt. angew. Ch., 1892, 653; Brunckow, Ch. News, 1, 1860, 98; Clevenger, Met. Ch. Eng., 14, 1916, 203. (Production) Merrill, C.A., 24, 1930, 4490. (Density) Stahl, C.A., 16, 1922, 3240. (Sterling silver) Downs, Jl. Soc. Ch. Ind., 46, 1927, 581; Smith, *ibid.*, 48, 1929, 931. (Uses) Brinn, C.A., 24, 1930, 4497; McDonald, Jl. Soc. Ch. Ind., 50, 1931, 168.

Silver Oxides.—Wislicenus, B., 4, 1871, 63; Lundy, C.A., 23, 1929, 2896.

Silver Nitrate.—(History) Herapath, A.J.P., 26, 1854, 62; Silberrad, Jl. Soc. Ch. Ind., 42, 1923, 925. (Manufacture) Procter, A.J.P., 36, 1864, 301; Anon., C.A., 19, 1925, 1180. (Blackening) Newbury, Am. Ch. Jl., 8, 1886, 196; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1155. (Removing stains) Edwards, Pacific Pharm., 3, 1910, 88; Anon., Pract. Dr., 47, Dec., 1929, 34. (Pills) Franck, Ap. Zt., 27, 1913, 232.

Photography.—Butterfield, A.J.P., 61, 1889, 45; Trivelli, Ch. Cent., 82, 1911, 707; Mees, Sigma Xi Quart., 19, 1931, 1.

Lunar Caustic.—(History) Wootton, 1, 1910, 424. (Preparation) Hughes, Proc. P.P.A., 45, 1922, 208.

Mitigated Caustic.—(Manufacture) Anon., A.J.P., 49, 1877, 373; Maisch, A.J.P., 55, 1883, 347.

Silver Cyanide.—Duhamel, A.J.P., 12, 1840, 186.

Silver Iodide.—(Manufacture) Deville, Gmelin-Kraut, 5^2, 1908, 115. (Emulsion) Thum, A.J.P., 82, 1910, 507 and 87, 1915, 500.

Silver Oxide.—(Manufacture) Stas, Gmelin-Kraut, 5^2, 1908, 41; Lane, Ph. Jl., 6, 1846, 170. (Explosive character) Smith, A.J.P., 31, 1859, 308; Witzemann, Jl. Ind. Eng. Ch., 11, 1919, 893.

Fulminating Silver.—Anon., Am. Dr., 25, 1894, 424; Siverts, Zt. angew. Ch., 22, 1909, 16; Burgess, A.J.P., 14, 1842, 163; Draper, A.J.P., 59, 1887, 22.

Silver Proteins.—(Manufacture) Lea, Ch. Cent., 60, ii, 1889, 315. Paal, Jl. Soc. Ch. Ind., 21, 1902, 916; Gerasimov, C.A., 23, 1929, 1719. (Properties) Stephenson, A.J.P., 96, 1918, 595; Sollmann, Jl. A.Ph.A., 7, 1918, 677. Giesy and Smith, Jl. A.Ph.A., 14, 1925; 10; Kolthoff, *ibid.*, 14, 1925, 183; Sollmann and Pilcher, C.A., 19, 1925, 538; Mannich and Curtaz, Arch. d. Pharm., 263, 1925, 669; Anon., Jl. A.M.A., 87, 1926, 430; Giesy, Jl. A.Ph.A., 19, 1930, 8 to 10; Samaan, Quart. J. Pharm., 3, 1930, 21. (Dispensing) Andrews, Jl. A.Ph.A., 19, 1930, 1098; Anon., Ph. Jl., 128, 1932, 282. (Deterioration) Stephen, Ap. Zt., 27, 1912, 148; Anon., Jl. A.M.A., 71, 1918, 1086; Culver, C.A., 12, 1918, 2374; Sollmann and Pilcher, see above; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1155. (Removing stains) Clare, Dr. Circ., 54, 1910, 410.

PART IV

ORGANIC CHEMISTRY

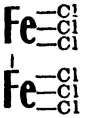
CHAPTER XXXV

FUNDAMENTAL PRINCIPLES

ORGANIC chemistry is the study of the carbon compounds, the adjective "organic" being a survival of the earlier days of chemical thought, when it was supposed that all substances peculiar to animal and vegetable economy—such bodies as those about to be discussed—were produced in animal or plant organs by the action of a mysterious influence called the force of life—"*vis vitæ.*" Although this vis vitæ theory was exploded in 1828 by Woehler's synthesis of urea (p. 756), the name "organic chemistry" is still applied to the carbon compounds.

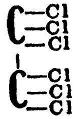
Essential to an organic compound are the carbon atoms it contains, and it is interesting to note that in all the numberless derivatives of carbon (some 355,000 now known to the practice) these carbon atoms always show the valence IV, just as do the carbon atoms in the carbonates discussed in previous chapters.

The reason why carbon forms so many compounds is because it possesses, to a far greater extent than any other element, the property of using some of its bonds for linking itself to adjoining carbon atoms. That one atom of an element is capable of attaching itself to another atom of the same element has been already shown, for example, in the formula Fe_2Cl_6 (p. 559), the graphic formula showing that two atoms of iron are directly attached to each other. Likewise in Hg_2Cl_2 the two mercury atoms are attached to each other by their own bonds. Returning to the question of ferric chloride, it will be remembered that its formula was explained by the statement that we had iron with the valence IV, and with a bond of each iron atom used for attaching itself to the other, as shown in graphic formula:



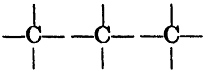
$$\begin{array}{l}\mathrm{Fe}\begin{smallmatrix}-\mathrm{Cl}\\-\mathrm{Cl}\\-\mathrm{Cl}\end{smallmatrix}\\ \;| \\ \mathrm{Fe}\begin{smallmatrix}-\mathrm{Cl}\\-\mathrm{Cl}\\-\mathrm{Cl}\end{smallmatrix}\end{array}$$

Exactly analogous to ferric chloride is the formula of ethane, that carbon compound containing two atoms, and, as a matter of fact, there is known a body C_2Cl_6, exactly analogous to Fe_2Cl_6:



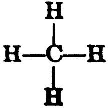
$$\begin{array}{l}\mathrm{C}\begin{smallmatrix}-\mathrm{Cl}\\-\mathrm{Cl}\\-\mathrm{Cl}\end{smallmatrix}\\ | \\ \mathrm{C}\begin{smallmatrix}-\mathrm{Cl}\\-\mathrm{Cl}\\-\mathrm{Cl}\end{smallmatrix}\end{array}$$

These two carbon atoms, however, can link on a third carbon atom, making a chain of three carbon atoms, which can be graphically represented as:

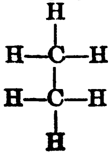


And in this way there can be devised chains containing four, five, or six carbon atoms, making the following series:

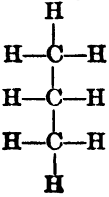
METHANE. CH_4



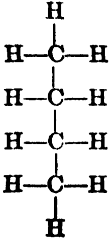
ETHANE. C_2H_6



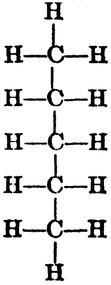
PROPANE. C_3H_8



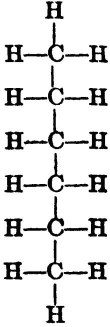
BUTANE. C_4H_{10}



PENTANE. C_5H_{12}



HEXANE. C_6H_{14}



This series can be continued almost indefinitely, similar chains containing 94 carbon atoms being known.

These compounds are composed only of carbon and hydrogen, and are called *hydrocarbons*. They all belong to a similar set or series, and the members of such a series are called *homologues*. In this series of homologues the carbon atoms are linked into a long string or chain, and the series is called the *chain series* of hydrocarbons. Because these hydrocarbons and their derivatives are found in fats, the series is sometimes called the *fatty series*.

Among the members of the series there exists a mathematic relationship between the relative number of carbon and hydrogen atoms.

This relationship can be expressed in the mathematic formula C_nH_{2n+2}, which means twice the number of carbon atoms, plus two, gives the number of hydrogen atoms.

Let us prove this:

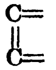
Take methane, CH_4. There is one carbon—C_n means C.
H_{2n+2} means $2 \times 1 = 2$; $2 + 2 = 4$, H_{2n+2} means H_4.

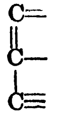
So with ethane, C_2H_6. C_n means C_2.
H_{2n+2} means $2 \times 2 = 4$; $4 + 2 = 6$, H_{2n+2} means H_6.

Likewise with propane, C_3H_8. In this case C_n means C_3.
H_{2n+2} means $2 \times 3 = 6$; $6 + 2 = 8$, H_{2n+2} means H_8.

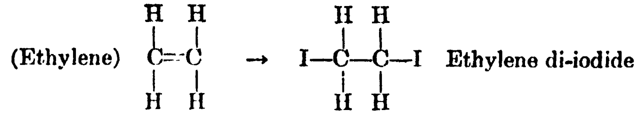
Lastly the hydrocarbon, $C_{60}H_{122}$. In this case C_n means C_{60}.
H_{2n+2} means $2 \times 60 = 120$; $120 + 2 = 122$; H_{2n+2} means H_{122}.

In methane, ethane, propane, and the other hydrocarbons, possessing the general formula, C_nH_{2n+2}, the carbon atoms are arranged in a chain, that is, one linked after another, like beads on a string. Another variety of chain hydrocarbons are those having the formula C_nH_{2n}, of which ethylene and propylene are the types. These bodies are unsaturated, that is, at least two of the carbon atoms of the compound are linked together by means of double bonds, as outlined in the graphic formula:



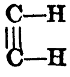


These are said to be unsaturated, because the double bonds split whenever opportunity is presented for them to be used for attaching other elements to the carbon atom. Thus, if ethylene is treated with iodine, the double bond is immediately severed and an iodine atom is attached to each bond, making ethylene di-iodide, as shown in the following graphic formula:

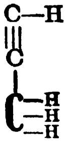


$$\text{(Ethylene)}\ \underset{H}{\overset{H}{C}}=\underset{H}{\overset{H}{C}} \rightarrow I-\underset{H}{\overset{H}{C}}-\underset{H}{\overset{H}{C}}-I\ \text{Ethylene di-iodide}$$

Another series of chain hydrocarbons is the acetylene series, in which adjoining carbon atoms are connected by a triple bond, as shown in acetylene and allylene, graphic formulas of which are given:



Acetylene



Allylene

Besides these chain series of hydrocarbons, we have a series of hydrocarbons of which benzene, C_6H_6, is the type, in which the carbon atoms form a ring, as explained on p. 767. This series is called the aromatic series, in contradistinction to the fatty series of chain hydrocarbons just cited.

Radicals are atomic groups, either organic or inorganic, not existing in a free state, but assigned names, and temporarily considered as entities, merely for convenience.

Chemists run across scores of chemical compounds containing the group, say, C_2H_5 (examples: C_2H_5OH, or alcohol; $(C_2H_5)_2O$, or ether, etc.), and as many others containing, say, COOH. Neither C_2H_5 nor COOH exists in a free state, but since we meet them so often in compounds, we give them names. Thus, we call C_2H_5 "*ethyl*," simply because it is much easier to say "ethyl" than to call the compound "two atoms of carbon and five atoms of hydrogen," and for similar reason we call COOH "*carboxyl*." Such atomic groupings are called radicals.

In methane, CH_4, we have a body in which all the bonds of the carbon are taken up by hydrogen. In all known bodies the employment of all the bonds of the carbon atoms, in some way or other, is distinctly noticeable, and carbon compounds having free bonds are not believed to exist.

As already mentioned, free atoms do not exist; yet free atoms enter into chemical combinations. Such is the case with what are called radicals, and of these, we may take as example the group CH_3, which we call methyl.

Lately, Gomberg through his work on what he calls "trivalent carbon" challenges the classic statement just given. Paneth and his coworkers claimed to have isolated the free radical, methyl; while Pearson and his coworkers confirm Paneth's work and announce the isolation of free ethyl. These free radicals exist, however, during less than one hundredth of a second.

Note that $C\begin{smallmatrix}-H\\-H\\-H\end{smallmatrix}$ has a free bond, hence it does not exist in a free state. But as it enters into chemical reactions, we may consider it just as we do atoms.

For instance, just as sodium (Na) and chlorine (Cl) join to form sodium chloride (NaCl), so is obtained CH_3Cl, which is called methyl chloride.

Just as the radical CH_3 is considered as a derivative of CH_4, so from C_2H_6 is derived the radical *ethyl*, C_2H_5, and from C_3H_8 the radical C_3H_7, which is called *propyl*.

Another similarity between atoms of elements and radicals.

Elements are divided into positive and negative, according as their action resembles metals or nonmetals.

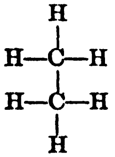
The radicals mentioned thus far are all typical of a character somewhat similar to metals, since each (CH_3, for example) combines with chlorine, just as sodium or iron does. Others there are that act like the negative part of the molecule; such groups as (OH), (COOH), and (CHO) resembling negative elements.

It is important to remember that combinations of such radicals do not as a rule ionize, whereas compounds of which metals are a part readily ionize.

But too much trust must not be placed on this idea of radicals, as the following facts show that they should be considered more as a convenient figure of speech than as definite chemical entities.

Na, the atom of sodium, does not exist in a free state; Na_2, the molecule, does (graphically expressed, Na—Na), the atoms linked "hand in hand."

Methyl, the radical CH_3, does not exist in a free state; $(CH_3)_2$ does, but as a body entirely different from the hypothetic methyl, from which it is derived.



$$CH_3\text{—}CH_3 \text{ is } \begin{array}{c} H \\ | \\ H\text{—}C\text{—}H \\ | \\ H\text{—}C\text{—}H \\ | \\ H \end{array} C_2H_6 \text{ (Ethane),}$$

which, when brought in contact with chlorine, does not form CH_3Cl (as Na_2 treated with chlorine yields NaCl), but the product is C_2H_5Cl.

Another difference is that the atom of an element is unchangeable: methyl, the radical, can be modified from $(CH_3)^I$ to $(CH_2Cl)^I$, $(CHCl_2)^I$, or $(CCl_3)^I$, and exactly so with all other radicals.

The Roman numeral outside the brackets in each formula means that the radicals have as many free bonds as the numeral indicates.

Further discussion of radicals is beyond the limits of this book, and in conclusion there will only be added the statement that the name of each radical is given the termination "*yl.*"

The following are the more important radicals:

Positive				Negative
Methyl	$(CH_3)^I$,	from methane,	CH_4.	Hydroxyl $(OH)^I$.
Ethyl	$(C_2H_5)^I$,	from ethane,	C_2H_6.	Carboxyl $(COOH)^I$.
Propyl	$(C_3H_7)^I$,	from propane,	C_3H_8.	Carbonyl $(CO)^{II}$.
Butyl	$(C_4H_9)^I$,	from butane,	C_4H_{10}.	The Aldehyde Radicle, $(CHO)^I$.
Amyl	$(C_5H_{11})^I$,	from pentane,	C_5H_{12}.	
Phenyl	$(C_6H_5)^I$,	from benzene,	C_6H_6.	

In considering the chemistry of the official organic substances, it is found convenient first to discuss the hydrocarbons themselves, and then the vast mass of derivatives, and in this work the order of the consideration of the latter will be based on a convenient standard of the number of carbon atoms they contain. In special books on organic chemistry it is usual to consider the derivatives of the hydrocarbons in groups, based on their structural characteristics; thus, all the fatty alcohols are considered together, likewise the fatty aldehydes and acids, but, from the pharmacist's point of view, it is better to discuss them in a different arrangement; namely, to study all the derivatives of ethane together, and then proceed to propane.

A convenient grouping of the derivatives is as follows:

The Halogen Derivatives.—In this case the hydrogen atoms are replaced by the halogen elements, chlorine, bromine, iodine. Thus, from CH_3 we can get CH_3Cl, CH_2Cl_2, $CHCl_3$, and CCl_4.

The first three of these can be expressed by the formulas:

$$R^IX,\ R^{II}X_2,\ \text{and}\ R^{III}X_3.$$

R standing for the radical, X for the appropriate halogen element, the Roman numerals above R expressing the number of free bonds the same possesses.

Methane treated with bromine yields respectively—

$$CH_3Br,\ CH_2Br_2,\ CHBr_3,\ CBr_4,$$

and such is the case with iodine. Likewise, with ethane, one or even all of the six hydrogen atoms can be replaced with chlorine, bromine, or iodine.

Of these halogen derivatives chloroform, bromoform, and iodoform are of pharmaceutic interest.

The Alcohols.—The formulas of these can be expressed by:

$$R^IOH,\ R^{III}(OH)_3,\ R^{VI}(OH)_6,\ \text{etc.}$$

Alcohols are substitution products of the hydrocarbons, in which one or more of the hydrogens are replaced by hydroxyl groups (OH). Official examples of this class are:

Ethyl alcohol	C_2H_5OH.
Glycerin	$C_3H_5(OH)_3$.
Mannitol	$C_6H_8(OH)_6$.

These alcohols are divided into primary, secondary, and tertiary alcohols, being classified according to their action under the influence of oxidation.

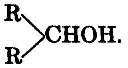
A *primary alcohol* oxidizes to an aldehyde and then to an acid; thus, ethyl alcohol, CH_3CH_2OH, on being treated with an oxidizing agent, yields first an aldehyde, CH_3CHO, and finally the acid, CH_3COOH.

A general formula of a primary alcohol shows as distinguishing characteristic the group RCH_2OH, that is, the carbon atom to which the hydroxyl is attached has also attached one radical and two hydrogen atoms.

A *secondary alcohol*, on oxidation, does not yield an aldehyde and then an acid, but yields a substance called a ketone.

Thus, secondary propyl alcohol, $CH_3CHOHCH_3$, yields on oxidation the ketone, acetone, CH_3COCH_3.

The rational formula of a secondary alcohol shows the characteristic grouping—



$$\begin{matrix}R\diagdown \\ \quad >CHOH. \\ R\diagup\end{matrix}$$

In other words, connected with the carbon atom to which the hydroxyl is attached are found two radicals and only one hydrogen atom.

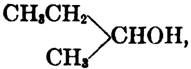
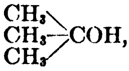
A tertiary alcohol is one which, on oxidation, yields neither an aldehyde nor a ketone, but breaks up under such treatment. The rational formula of tertiary alcohol can best be expressed as—

$$R_3COH;$$

in other words, to the carbon atom to which the hydroxyl is attached there are fastened three radicals and no hydrogen atoms at all.

Perhaps the differentiation in the three classes of alcohols can better be understood by a comparison of three such alcohols from the same hydrocarbon and the oxidation derivatives of each.

Thus, primary butyl alcohol, $CH_3CH_2CH_2CH_2OH$, yields on oxidation, butyric aldehyde and butyric acid.

Secondary butyl alcohol,  $\begin{matrix}CH_3CH_2\diagdown \\ \quad >CHOH, \\ CH_3\diagup\end{matrix}$ under same treatment, yields methylethylketone, while tertiary butyl alcohol,  $\begin{matrix}CH_3\diagdown \\ CH_3-COH, \\ CH_3\diagup\end{matrix}$ breaks down into simpler compounds.

Another classification of alcohols, not frequently used, is the monatomic, diatomic, and triatomic, etc., the Greek prefixes signifying the number of hydroxyls the alcohol possesses: thus glycerin, $C_3H_5(OH)_3$, is a triatomic alcohol.

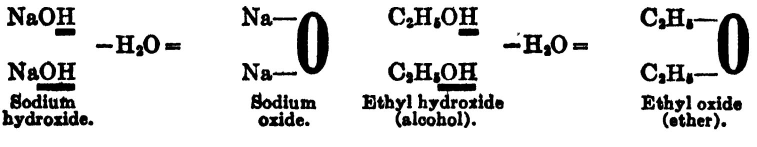
It will be seen that the characteristic radical of alcohols is hydroxyl (OH). To express the same thing differently, alcohols are hydroxides of the organic radicals, just as the bases (p. 394) are inorganic hydroxides.

Thus, NaOH, sodium hydroxide, has an organic analogue in C_2H_5OH, ethyl hydroxide. Similar to $Ca(OH)_2$, calcium hydroxide, is $C_2H_4(OH)_2$, glycol, and as mate to $Fe(OH)_3$, ferric hydroxide, we have the organic hydroxide, $C_3H_5(OH)_3$, glycerin. Couch and other writers point out, however, that there is a marked difference between metallic hydroxides and alcohols.

All three organic hydroxides cited above are classed among the alcohols. Those alcohols formed by adding hydroxyl to the benzene group of radicals (C_6H_5, C_6H_4, etc.) are called *phenols*, of which the type is ordinary phenol, carbolic acid, C_6H_5OH.

As alcohols represent organic hydroxides, so the class of *ethers* represent organic oxides. In a preceding chapter (p. 394) it was noted that sodium hydroxide, NaOH, was evolved from sodium oxide, Na_2O, by adding water thereto. Likewise, by taking water away from sodium hydroxide, sodium oxide is produced. In a somewhat analogous way, by removing water from ethyl hydroxide (alcohol), ethyl oxide (ether) is formed.

Let us compare the formation of the two:



$$\begin{matrix}NaOH \\ NaOH\end{matrix} - H_2O = \begin{matrix}Na- \\ Na-\end{matrix}\Big\rangle O \qquad \begin{matrix}C_2H_5OH \\ C_2H_5OH\end{matrix} - H_2O = \begin{matrix}C_2H_5- \\ C_2H_5-\end{matrix}\Big\rangle O$$

The general formula of ethers can, therefore, be expressed as R^1OR^1.

Esters may be defined as salts of the alcohols.

We have seen the analogy between hydroxides and alcohols; between oxides and ethers; let us now show the similarity between salts and esters. Suppose we take sodium hydroxide and add nitrous acid, we get water and sodium nitrite:

$$\begin{array}{rccccccc} & NaOH & + & HNO_2 & = & H_2O & + & NaNO_2 \\ \text{Even so} & C_2H_5OH & + & HNO_2 & = & H_2O & + & C_2H_5NO_2 \\ & \text{Ethyl hydroxide.} & & \text{Nitrous acid.} & & & & \text{Ethyl nitrite.} \end{array}$$

An ester is the combination of a positive organic radical with an acid radical, just as a salt is a combination of a positive element with an acid radical. The acid of the ester, just like the acid of the salt, can be either inorganic or organic, as is shown by the formulas of the official esters:

Ethyl nitrite	$C_2H_5NO_2$.
Ethyl acetate (acetic ether)	$C_2H_5C_2H_3O_2$.
Amyl nitrite	$C_5H_{11}NO_2$.
Phenyl salicylate (salol)	$C_6H_5C_7H_5O_3$.
Methyl salicylate	$CH_3C_7H_5O_3$.

Emphasis should be laid on the fact that esters are not in every respect similar to inorganic salts, a most striking difference being that while inorganic salts in solution dissociate into ions (p. 141), esters scarcely undergo ionic dissociation. Again, reaction of manufacture of esters (called *esterification*) occurs only in the presence of an acid (see p. 664) which acts either as a dehydrator or as a catalyst. Another point of difference is that, while the reaction occurring in the manufacture of salts usually runs in one direction, viz.,

$$2NaOH + H_2SO_4 = Na_2SO_4 + H_2O,$$

the ester reaction is reversible, viz.,

$$\begin{array}{ll} (a) & C_2H_5OH + HNO_2 = C_2H_5NO_2 + H_2O \\ (b) & C_2H_5NO_2 + H_2O = C_2H_5OH + HNO_2. \end{array}$$

The latter reaction, whereby esters are dissociated, is called the process of *saponification*.

Aldehydes.—This class of organic compounds has no analogues among the inorganic compounds, it being the product of the oxidation of a primary alcohol. An explanation of the same has just been given under the classification of the alcohols, and specific details will be left until we consider the official aldehydes; so here suffice it to say that the general formula of aldehyde is RCHO. An example of the official aldehydes is benzaldehyde, the chief constituent of oil of bitter almond.

Ketones.—As mentioned above, ketones are oxidation products of secondary alcohols, and their general formula is R_2CO. Thus, the secondary propyl alcohol, $CH_3CHOHCH_3$, under influence of oxidizing agents, loses the two hydrogen atoms, becoming CH_3COCH_3, the official acetone.

Acids.—The true organic acids are the oxidation products of primary alcohols or aldehydes, and their general formula is RCOOH, the group COOH being called *carboxyl*, as mentioned on p. 633.

As alcohols are monatomic, diatomic, and triatomic, according to the number of hydroxyls, so organic acids are monobasic, dibasic, and tribasic, according to the number of carboxyls they contain. Thus, acetic acid is an official example of the monobasic organic acid, while succinic acid, $C_2H_4(COOH)_2$, is an illustration of a dibasic acid.

Acids with alcohol radicals, that is, containing carboxyl and hydroxyl, are called *oxy-acids*, and an official illustration is furnished in tartaric acid, which is a dibasic, diatomic oxy-acid, as shown by the graphic formula. (See p. 684.)

Gerock considers carbonic acid as an organic oxy-acid, viz.,

$$\begin{array}{l} OH \\ | \\ COOH \end{array}$$

In true acids only those hydrogen atoms in carboxyl groups are replaceable by a metal. This is why carbolic acid (C_6H_5OH) is not a true acid, but a phenol (p. 771).

Amines can be expressed by the general formulas—

$$RNH_2,\ R_2NH, \text{ or } R_3N.$$

They can also be considered as ammonia in which one, two, or three hydrogens have been replaced by radicals. Thus we can obtain methylamine, CH_3NH_2, dimethylamine, $(CH_3)_2NH$, and trimethylamine, $(CH_3)_3N$.

The manufacture of these products is so simple and clear that it serves admirably for explaining their exact composition. Thus ammonia treated with methyl iodide gives the hydriodic acid salt of methylamine, and when the acid is removed by treating with potassa, methylamine remains.

Reaction: (*a*) $NH_3 + CH_3I = NH_2CH_3HI.$
(*b*) $NH_2CH_3HI + KOH = NH_2CH_3 + KI + H_2O.$

Methylamine, being treated with methyl iodide, will yield the hydriodic acid salt of dimethylamine, and this by treatment with potassa yields the free dimethylamine.

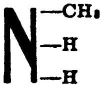
Reaction: (*a*) $NH_2CH_3 + CH_3I = NH(CH_3)_2HI.$
(*b*) $NH(CH_3)_2HI + KOH = NH(CH_3)_2 + KI + H_2O.$

Dimethylamine, being treated with methyl iodide, yields the hydriodic acid salt of trimethylamine, and the free base is obtained by treatment with potassa as above. Lastly, if trimethylamine is treated with methyl iodide, we get a very interesting body called tetramethylammonium iodide.

Reaction: $N(CH_3)_3 + CH_3I = N(CH_3)_4I.$

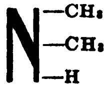
In the latter case the nitrogen shows the valence v, exactly as it does in the ammonium compounds. The similarity of these four bodies, the amines and the ammonium compounds respectively, is best shown by comparison of the four graphic formulas:

Methylamine.



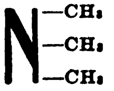
$NH_2CH_3.$

Dimethylamine.



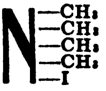
$NH(CH_3)_2.$

Trimethylamine.



$N(CH_3)_3.$

Tetramethyl ammonium iodide.



$N(CH_3)_4I.$

It might be added that for methyl can be substituted ethyl, propyl, or any other monovalent radical. All the amines are quite similar to ammonia; the mono-amines have ammoniacal odor and all are decidedly basic.

The amines of the fatty series are of but little importance, but several of the aromatic series are of great value; for example, aniline (p. 779).

CHAPTER XXXVI

HYDROCARBONS AND METHANE DERIVATIVES

THE FATTY SERIES OF HYDROCARBONS

THIS series of hydrocarbons, having the general formula C_nH_{2n+2}, is sometimes called the *aliphatic series*. As mentioned in the preceding chapter, representatives of these series are the homologues, methane, ethane, butane, pentane, hexane, etc., all similar and manufactured one from the other. Substances possessing the same general formula, but differing in relative number of atoms, are called *homologues*.

Manufacture.—That the members of this class can be made one from the other has already been mentioned; thus, methane, CH_4, can be converted into methyl iodide, (CH_3I), and methyl iodide, on treatment with metallic sodium, yields ethane by the following reaction:

$$2CH_3I + Na_2 = 2NaI + CH_3—CH_3 \text{ or } C_2H_6.$$

This is the usual way of making such hydrocarbons, although several other methods have been devised.

Chemical Behavior.—These hydrocarbons are saturated bodies; that is, they will absorb no more hydrogen nor will they combine with halogens except through the loss of hydrogen atoms. The halogen derivatives are formed as follows:

$$CH_4 + Cl_2 = CH_3Cl + HCl.$$
$$CH_3Cl + Cl_2 = CH_2Cl_2 + HCl.$$
$$CH_2Cl_2 + Cl_2 = CHCl_3 + HCl.$$
$$CHCl_3 + Cl_2 = CCl_4 + HCl.$$

Physical Properties.—The first of these series of hydrocarbons are gases. Hydrocarbons from C_6H_{14} are liquids, the first being quite volatile, the higher ones, that is, from $C_{14}H_{30}$, thick and stable liquids, while the higher hydrocarbons of the series, say from $C_{20}H_{42}$, are solid.

Considering the hydrocarbons as individuals, the first of the series, *methane*, CH_4, is commonly called *marsh gas*, because formed by decaying vegetable matter, and thus it can be easily collected from the surfaces of some marshes. It is the chief constituent of natural gas. Methane is usually made by heating in a retort sodium acetate with sodium hydroxide, as shown in the following equation:

$$CH_3COONa + NaOH = CH_4 + Na_2CO_3.$$

It can also be prepared spontaneously by immersing zinc methyl in water, as shown in the following equation:

$$Zn(CH_3)_2 + H_2O = 2CH_4 + ZnO.$$

The zinc methyl used is made by heating together methyl iodide and zinc and distilling over the zinc methyl in the presence of absolutely dry hydrogen, the reaction being:

$$2CH_3I + Zn_2 = Zn(CH_3)_2 + ZnI_2.$$

Ethane, C_2H_6, can be made as cited above, by treatment of methyl iodide with metallic sodium. It can also be made by treating sodium propionate with sodium hydroxide in a manner similar to the method given for making methane from sodium acetate, the reaction being as follows:

$$CH_3CH_2COONa + NaOH = CH_3CH_3 + Na_2CO_3.$$

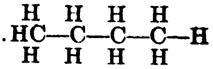
Propane, C_3H_8, is made by treating a mixture of methyl iodide and ethyl iodide with metallic sodium, the reaction being as follows:

$$CH_3I + C_2H_5I + Na_2 = 2NaI + CH_3—C_2H_5 \text{ (or } C_3H_8).$$

Butane, C_4H_{10}, is interesting, inasmuch as two substances of this formula—C_4H_{10}—are known. Already we have learned that where an element is found in two or three different forms, such forms are said to be allotropic (p. 428). On the other hand, where several compounds differ physically, but have the same chemical formula, they are called *isomeres*, and in organic chemistry a vast number of such isomeres are found, the two types of butane being the first example we meet. The two types of butane can best be described by submitting the graphic formula, and it will be found, on careful calculation, that these are the only two possible combinations of the formula C_4H_{10}.

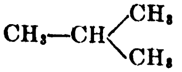
The two butanes are:

Normal......................

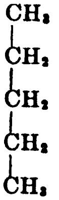


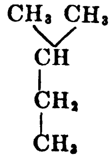
$$\begin{array}{c} \mathrm{H}\quad\mathrm{H}\quad\mathrm{H}\quad\mathrm{H} \\ \mathrm{HC{-}C{-}C{-}C{-}H} \\ \mathrm{H}\quad\mathrm{H}\quad\mathrm{H}\quad\mathrm{H} \end{array}$$

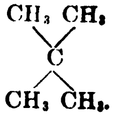
Isobutane......................



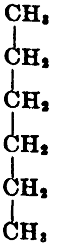
Pentane, C_5H_{12}, can occur in three different forms, namely:

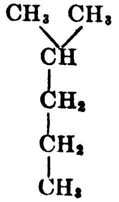


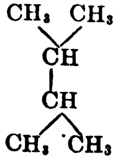


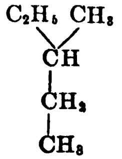


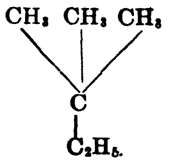
Hexane, C_6H_{14}, exists in five possible combinations, namely:











and all of these are known.

It will be seen from the above that the number of isomeres increases in proportion to the number of carbon atoms which the compound possesses, and in bodies containing a large number of carbon atoms the possible number of isomeres is enormous. Thus, Perry calculates that the possible number of isomeres of $C_{40}H_{122}$ is over 22 sextillion.

Of the hydrocarbons beyond hexane, such as C_7H_{14} and C_8H_{16}, nothing need be said beyond the fact that the formula of each can be worked out from the general formula C_nH_{2n+2}, as explained on p. 632.

The hydrocarbons above cited are of interest pharmaceutically because they are constituents of natural gas and of the petroleum products, and these we will now discuss.

Natural gas is chiefly methane combined with ethane and other hydrocarbons. It is found in pockets beneath the surface of the earth, from which it is extracted by drilling, as in artesian wells, until the pocket is reached, when the gas rushes out and is piped to places where it is desired to be used. The city of Chicago is furnished with natural gas brought from Texas 1000 miles away.

Petroleum is a thick, greasy liquid, obtained from pockets beneath the earth by drilling, as in the case of natural gas—in fact, the two are usually associated. The chief localities in which petroleum is obtained are Pennsylvania and the Central Western States (Ohio, Indiana, West Virginia), Texas, California, in the neighborhood of Baku, South Russia, and in Mexico.,

Petroleum was first drilled for in Venango County, Pennsylvania, in 1859, although the oil which oozed from the earth was known by the Indians two hundred and fifty years ago. The Russian fields have been worked commercially once since the Pennsylvania fields have been operated, while the Texas fields were opened in 1900. In 1930, the world's petroleum production was almost 1½ billion barrels of which over 1 billion barrels were produced in the United States. Of this, about 525 million barrels came from the California and Oklahoma fields.

Petroleum is supposed to be the result of the decomposition of decaying fishy matter, the geological explanation of the limited areas where found being that in each case the pockets represent some sea that disappeared, these cataclysms of nature leaving the fishy denizens to be engulfed beneath masses of rock. Other theories are that vegetable matter under the influence of heat and pressure has decomposed to petroleum; while Moissan claimed that it was produced from inorganic material, that carbides were produced by the action of metals on carbon and that these combined with water under pressure to form the hydrocarbons of which petroleum is composed.

Of the petroleums, that of Pennsylvania and adjoining states is the best, the Russian containing sulfur, which must be removed from the distillate before it can be used for fuel or light, while the Texas petroleum contains a lesser amount of the lower boiling products and contains 1.4 to 1.8 per cent sulfur. As mentioned above, the process of extracting petroleum from the earth is simple, consisting merely of driving an artesian well, and when the bed rock is reached, exploding the rocky layer with nitroglycerin. The depth of this rocky layer varies, some wells being 8000 feet deep.

When the free petroleum rushes through the tube to the earth's surface, it is with a pressure, more or less great, depending on the amount of gas mixed with petroleum. When first opened, in 1915, a "spouter" near Tampico, Mexico, attained the height of 600 feet.

At first the gas pressure is sufficient to cause a large flow of petroleum; in fact, in some cases the difficulty is properly to control the flow. After flowing a while, however, the pressure diminishes, until finally recourse must be had to pumps.

Petroleum, as it emerges from the earth, is a dark, greasy liquid of disagreeable odor. This forms "*stone oil*," which was formerly in considerable esteem medicinally as a liniment. Upon distillation this "crude oil" yields a large variety of products which may be generally classified as follows:

1. Gases, such as methane and ethane.
2. Rhigolene, chiefly C_5H_{12}, boiling point, 10° C.
3. Gasoline (benzin) chiefly C_5H_{12} and C_6H_{14}, boiling point 50° to 60° C.
4. Insurance oil (coal oil, etc.) C_7H_{16}, C_8H_{18}, etc., boiling point, 60° to 100° C.

The several distillation fractions are purified by agitation with concentrated sulfuric acid and redistillation. From the residue remaining after distillation are obtained:

5. Liquid petrolatum, U.S.P.
6. Petrolatum, U.S.P.
7. White petrolatum, U.S.P.
8. Paraffin, U.S.P.

The separation of these is explained on p. 642.

Texas, Mexican and Californian petroleum differ markedly from the Pennsylvania oil just described. None of these contain large amounts of the lower boiling hydrocarbons that constitute gasoline and the thick viscid liquid is of value chiefly as lubricating and fuel oils. Such types of petroleum are now being successfully "*cracked*;" that is, when these fuel oils are heated under a pressure of 90 pounds to the square inch, gasoline and even benzene (p. 770) may be produced.

Rhigolene has been suggested (on account of its great volatility) as a local anesthetic, it freezing the surface on which it is sprayed. However, ethyl chloride is said to be better for this purpose.

Benzinum (U.S.P. VIII), or *Petroleum Ether*, is not the same as commercial benzin, which consists chiefly of higher boiling hydrocarbons. Even the phrase "petroleum ether" is not familiar to the average oil refiner, who calls the distillate approximating the official benzin, "88° naphtha." This phrase means a liquid has the specific gravity corresponding to "88 Baumé degrees light," which equals the specific gravity, 0.643.

Benzin was directed by U.S.P. VIII as a solvent for India rubber (when mixed with equal quantities of carbon disulfide), and was thus used in making mustard paper. Its value as a remover of grease spots is well known.

BENZINUM PURIFICATUM—Purified Petroleum Benzin

(Benzin. Purif.—Petroleum Ether)

Purified Petroleum Benzin is a purified distillate from petroleum, consisting of hydrocarbons, chiefly of the methane series.

Caution.—It is highly inflammable, and its vapor, when mixed with air and ignited, explodes violently.

Storage.—Preserve in well-closed containers, in a cool place, remote from fire.

Summarized Description.

Colorless, nonfluorescent, volatile liquid; ethereal, or petroleum-like odor; highly inflammable; vapor mixed with air is explosive; insoluble in water; soluble in alcohol; miscible with ether, chloroform, benzene, volatile and fixed oils (except castor oil); sp. gr. 0.634 to 0.660; distils between 35° and 80° C.

For details, see U.S.P., p. 85.

For *tests for identity*, and for *impurities* (other petroleum products; pyrogenous products, sulfur compounds, and benzene), see U.S.P., p. 85.

Remarks.—This represents the crude petroleum ether freed from other matter by oxidation with permanganate; the crude petroleum ether being shaken with an aqueous solution of potassium permanganate containing sulfuric acid and after separation from this fluid, it is shaken with an alkaline permanganate solution. It is directed for use by N.F. VI as a solvent in defatting strophanthus prior to making a tincture from this drug.

Gasoline in commerce is a term used synonymously with benzin, enormous quantities being now used as motive power in automobiling. It is obtained not only by distillation of petroleum but also from natural gas, by the "cracking" of fuel oil and by the treatment of heated coal with air and steam (Bergius). The various illuminating oils, such as *insurance oil, coal oil, kerosene* and *headlight oil,* are petroleum products distilling over between 60° and 150° C. The higher the boiling point, the safer is such an oil; as a matter of fact, the use of the lower boiling oils, such as benzin and gasoline, is dangerous, especially in wick lamps. The latter are sometimes found in lamp oils. To detect such adulteration there has been devised the so-called *"flash test,"* which consists in heating the sample in an appropriate apparatus and noting at what temperature the sample gives off inflammable vapors. Thus kerosene oil should have a flash test of 45° C.; that is, its vapors should not ignite until the oil is heated to that temperature.

On the other hand the flash test of astral oil is about 150° C.

The first distillate of these bodies is always impure, and must be purified by treatment with sulfuric acid and redistillation.

The pharmaceutic products, *liquid petrolatum* and *petrolatum,* are obtained from the residue after distillation. This residue is distilled in vacuo, and according to its consistence forms hard or soft petrolatum, the latter having been introduced by Robert Chesebrough in 1871 under the name of *"vaseline."* If, on the other hand, the purified residue is chilled and then expressed, the limpid oil flows out, forming *liquid petrolatum,* U.S.P., while the residue is the commercial *paraffin.* The purification in each case is accomplished by filtration through animal charcoal. *White petrolatum* is a specially purified form of petrolatum.

PETROLATUM LIQUIDUM—Liquid Petrolatum

(Petrolat. Liq.—Liquid Paraffin, White Mineral Oil)

A mixture of liquid hydrocarbons obtained from petroleum.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Two varieties. The *heavy* has the kinematic viscosity of not more than 0.381 at 37.8° C.; the *light* has the kinematic viscosity of not more than 0.370 at 37.8° C. *Both* are colorless, oily liquids; sp. gr., 0.828 to 0.905; little fluorescence; faint petroleum odor on heating; insoluble in water and alcohol; soluble in ether, chloroform, petroleum benzin and in fixed and volatile oils; dissolves camphor, menthol and thymol. For details, see U.S.P., p. 281.

For *tests for identity* and for *impurities* (solid paraffins, acid or alkali, carbonizable substances, sulfur compounds), see U.S.P., p. 281.

Remarks.—Liquid petrolatum is used for two purposes. It was originally introduced into medicine as a basis of atomizing fluids used in nose and throat troubles, in which antiseptics such as menthol, thymol, etc., were dissolved in the fluid. Of late years it has come into enormous use as a laxative. For the latter purpose a heavy liquid possessing considerable viscosity is required, whereas in atomizing a light fluid of low viscosity is indicated. The monograph of the present Pharmacopœia provides for both kinds and also gives a viscosity test (see above) which is worthy of study.

The best type of heavy liquid petrolatum contains naphthenes (see p. 768) rather than the hydrocarbons of the aliphatic series. Originally coming from Russia via Holland and sold in this country under the name of *Russian white oil*, its scarcity during the World War brought about a search for American substitutes. This search was rewarded by the discovery that certain Californian petroleums yielded white oils of as good quality as the Russian oil.

Dose.—15 cc. (4 fluidrachms).

PETROLATUM—Petrolatum

(Petrolat.—Petroleum Jelly)

A purified, semisolid mixture of hydrocarbons obtained from petroleum.

Summarized Description.

Unctuous mass; yellow to light amber; only slightly fluorescent: insoluble in water; almost insoluble in alcohol or in cold dehydrated alcohol; soluble in ether, chloroform, carbon disulfide, oil of turpentine, petroleum benzin, benzene and volatile and fixed oils; sp. gr. 0.820 to 0.865; melts between 38° and 54°. For details, see U.S.P., p. 280.

For *tests for identity* and for *impurities* (acids and alkalis, fixed oils, fats, rosin), see U.S.P., p. 280.

Remarks.—Petrolatum is commonly known as petroleum jelly and appears in commerce under the trade names of *vaseline*, *cosmoline*, *saxoline*, etc.

PETROLATUM ALBUM—White Petrolatum

(Petrolat. Alb.—White Petroleum Jelly)

Petrolatum wholly or nearly decolorized.

Summarized Description.

White or faintly yellow unctuous mass; completely amorphous; transparent in thin layers after cooling. Otherwise like petrolatum. For details, see U.S.P., p. 281.

Remarks.—White petrolatum represents a special form of solid petrolatum obtained from Russian petroleum. It was originally introduced in this country under the name of *albolene*. Since the European War, the Russian product has become very scarce in this country and fairly satisfactory American substitutes have been put upon the market. Most of these meet the requirements of the present Pharmacopœia.

A cheap form of white petrolatum, made by dissolving paraffin in liquid petrolatum in varying quantities, has been marketed. This, however, should never be used, as on standing it invariably becomes lumpy, due to separation of the paraffin. Meyer points out that there are at least three types of petrolatum, based upon consistency and that each type has its special use in pharmacy and in cosmetics.

These petroleum jellies are used as ointment bases, possessing over lard and other fats the great advantage of not turning rancid. Because of their greasy character, these jellies are usually grouped among the animal and vegetable fats, but from these the petroleum products differ entirely, the latter being the glycerin derivatives of oleic, stearic, and palmitic acids; their rancidity is due to the decomposition of these compounds (p. 729). This is, of course, impossible with petrolatum, which is a mixture of the hydrocarbons, and, like all hydrocarbons, are not easily decomposed, even by chemicals. In fact, the halogens are about the only substances which will combine directly with the hydrocarbons.

This chemical stability is of great advantage in so far as the absence of rancidity is concerned, but, on the other hand, in making ointments, its stability is in some cases disadvantageous. Thus, physicians sometimes prescribe alkalis with fats, with the intention of securing a form of soap. If, instead of the animal or vegetable fat, the physician prescribes a petrolatum product, the same results are not obtained and an unsightly mixture occurs. (See p. 1070.)

Another drawback to the use of petroleum jelly as an ointment base is the fact that it is by no means so easily absorbed by the skin as are the animal or vegetable fats.

Petrox Preparations.—Ointment bases consisting of petrolatum emulsified with a soap made from ammonia and oleic acid now enjoy considerable popularity. These are described on pp. 292 and 373.

PARAFFINUM—Paraffin
(Paraff.)

A purified mixture of solid hydrocarbons obtained from petroleum.

Summarized Description.

Colorless or white, more or less translucent masses; deposits crystalline from solutions; insoluble in water or alcohol, slightly soluble in dehydrated alcohol; soluble in the solvents mentioned under petrolatum; sp. gr. 0.900; melts between 50° and 57° C.; ignites on strong heat, depositing carbon; not affected by cold concentrated sulfuric or nitric acid. For details, see U.S.P., p. 276.

For *tests for identity* and for *impurities* (acids), see U.S.P., p. 276.

Remarks.—Paraffin consists of the hydrocarbons from $C_{24}H_{50}$ to $C_{27}H_{56}$, or possibly four times the formula just given. It has of late come into extensive use for such purposes as making wax paper, candles, and for the polishing of floors and other wood.

Like the liquid and soft petrolatums, it is practically impervious to ordinary chemicals. It can even be boiled with concentrated sulfuric acid without any change in its properties, this test being employed in examining beeswax to see if adulterated with paraffin (p. 746).

Ceresin is a purified form of *ozokerite*, a paraffin-like substance mined in Galicia.

PARAFFINUM CHLORINATUM—Chlorinated Paraffin
(Paraff. Chlorinat.—Chlorcosane)

Chlorinated Paraffin is a liquid paraffin which has been treated with chlorine.

Summarized Description.

Amber-yellow, clear, thick, oily, odorless liquid; insoluble in water; slightly soluble in alcohol; miscible with benzene, chloroform, carbon tetrachloride, and ether; sp. gr., 1.00 to 1.07. For details, see U.S.P., p. 277.

For *tests for identity* and for *impurities* (acids and alkalis, free chlorine, chloride, incomplete chlorination) see U.S.P., p. 277.

Remarks.—This official is a chlorinated paraffin containing chlorine in stable (nonactive) combination. It is used almost entirely as a solvent for dichloramine-T.

Ichthammol (N.F. VI), or *Sulfonated Bitumen*, or *ammonium ichthyol sulfonate* is the product that was introduced under the name of *ichthyol.* It is obtained by the distillation of "asphalt stone," a bituminous shale found in Tyrol. The distillate is sulfonated by treatment with concentrated sulfuric acid, and is then converted into the ammonium compound. Commercial ichthyol is a fluid form of the above compound and contains about 50 per cent of a mixture of ammonium ichthyol sulfonate and of ammonium sulfate. It contains about 10 per cent of sulfur. It is used largely in the treatment of skin diseases, both internally and externally. *Dose.*—0.2 Gm. (3 grains).

In the absence of Austrian ichthyol from the American market during the World War, a number of Italian and Japanese varieties of ammonium ichthyol sulfonate were sold under trade names. The Japanese Pharmacopœia recognizes the Japanese product requiring, however, less severe standards than those prescribed for ichthyol.

The compounds of methane of pharmaceutic interest are:

Methyl chloride	CH_3Cl.
Chloroform, U.S.P.	$CHCl_3$.
Bromoform, U.S.P. IX	$CHBr_3$.
Iodoform, U.S.P.	CHI_3.
Methyl alcohol	CH_3OH.
Formic acid	HCOOH.
Formaldehyde	HCHO.
Solution of formaldehyde, U.S.P.	contains 37 per cent HCHO.
Paraformaldehyde, U.S.P. X	$(HCHO)_3$.
Methyl salicylate, U.S.P.	$CH_3C_7H_5O_3$.

Methyl Chloride (CH_3Cl).—This is made by treating methyl alcohol with hydrochloric acid in the presence of zinc chloride (Grove's method), the zinc chloride being used as a dehydrator—that is, to remove the water. It is now produced commercially from *schlemp*, or the refuse in the beet-sugar manufacture. Methyl chloride is a colorless gas, and is put upon the market in liquid form which boils at 22° C., made by compressing the gas, and is used as a refrigerant, as a solvent in perfumery and in synthesis of dye stuffs. Its medicinal use is for the purpose of producing local anesthesia, by directing it in a stream upon the part desired to become benumbed, as was the case in rhigolene.

CHLOROFORMUM—Chloroform

(Chlorof.)

$CHCl_3$. Molecular weight, 119.38

Chloroform contains not less than 99 per cent and not more than 99.5 per cent of $CHCl_3$, the remainder consisting of alcohol.

Caution.—Care should be taken not to vaporize chloroform in the presence of a naked flame, because of the production of noxious gases.

Storage.—Preserve in well-stoppered bottles, in a cool place and protected from light. If cork stoppers are used, cover them with tin foil or other suitable material.

Summarized Description.

Clear, colorless mobile liquid; characteristic ethereal odor; burning sweet taste; soluble in 210 times its volume of water; miscible with alcohol, ether, benzene, petroleum benzin and with volatile and fixed oils; sp. gr. 1.474 to 1.478; volatilizes at low temperatures; boils at 61° C.; not inflammable but its heated vapor burns with a green flame. For details, see U.S.P., p. 119.

For *tests for identity* and for *impurities* (chlorides, free chlorine, carbonizable substances, odorous decomposition products, chlorinated decomposition products, aldehydes, ketones, phosgene), see U.S.P., p. 119.

Remarks.—Chloroform was discovered by Dr. Guthrie, of Jewettsville, N. Y., in 1831, and was considered merely as an interesting chemical specimen until after the discovery of anesthesia by Long in 1842, and the popularizing of the discovery by Wells (1844) and Morton (1846) when it was discovered that chloroform could be used for that purpose as well as could ether, and since that time it has been of untold benefit in alleviating suffering attendant upon surgical operations.

Chloroform is made by treating alcohol with chlorinated lime. Chlorinated lime is, as learned on p. 421, a loose combination of chlorine and the alkali, lime; chlorine acting on alcohol gives chloral, as will be learned on p. 666, and chloral in contact with an alkali gives chloroform.

As this method of manufacture is so similar to that of chloral, full explanation of the process had best be left until we consider that chemical. The same applies to the manufacture of a very pure chloroform by treatment of chloral with an alkali.

Of recent years a large amount of chloroform has been produced by the so-called "acetone process," patented by Michaelis, in which acetone is treated with chlorinated lime in the same way as in the alcohol process, the advantage of the acetone process over the alcohol process being that the yield is very good, about 200 per cent, and the product much purer than that yielded by the alcohol process. Equation showing the acetone process is as follows:

$$2(CH_3)_2CO + 3Ca(OCl)_2 = 2CHCl_3 + 2Ca(OH)_2 + Ca(C_2H_3O_2)_2.$$

The chloroform for anesthesia is always purified by treatment with sulfuric acid and redistillation.

Another method of obtaining absolutely pure chloroform is that of Pictet. Chloroform solidifies at −80° C., whereas all the other impurities are solidified at −70° C. Therefore the mixture is subjected to a temperature of −70° C., and the liquid chloroform is then poured off from the frozen impurities. It is also made electrolytically.

A very delicate test for chloroform is the so-called *isonitrile reaction*, this consisting of treating the chloroformic liquid with an amino-compound (for example, aniline) in the presence of an alkali, when the disgusting odor of the very poisonous gas, phenyl (or some other) isonitrile is evolved. This test is interesting as being equally valuable for identifying the amines, any of which can be employed in place of aniline. The equation showing the reaction is as follows:

$$C_6H_5NH_2 + CHCl_3 + 3KOH = C_6H_5NC + 3KCl + 3H_2O.$$

It will be noticed that the Pharmacopœia permits the presence of 1 per cent of alcohol, this being added to preserve same, it being found that pure chloroform decomposes. The fact that chloroform does undergo decomposition renders it necessary for the pharmacist to assure himself that the chloroform he dispenses for anesthesia is strictly pharmacopœial, for should a death result during anesthesia, one of the first things done by the physician is to investigate the purity of the chloroform, and if found impure, it will prove very disastrous to the reputation of the pharmacist dispensing same. Hence every sample of chloroform should be carefully tested according to the Pharmacopœia for chlorinated products and for empyreuma.

A very simple and satisfactory test for empyreuma is the sulfuric acid test: when a layer of chloroform is poured upon pure sulfuric acid, no coloration should take place at point of contact. A simple test for acidity in chloroform is the fact that pure chloroform does not attack a cork of a container. If, therefore, the cork softens or becomes yellow, it is a sure indication of the presence of acid. Of course, the accurate test for acidity is by the use of litmus paper.

Chloroform allowed to vaporize in the presence of artificial light or heat becomes oxidized, the reaction being:

$$CHCl_3 + \underset{\text{(From air)}}{O} = HCl + \underset{\text{(Phosgene)}}{COCl_2}.$$

Nicloux, on the other hand, thinks that the decomposition of chloroform by action of light and air produces carbon monoxide; while Clover believes that a peroxide, $\begin{matrix}Cl\\Cl\end{matrix}\!\!>C=O=O$, is formed. Be that as it may, it is a dictum in surgery that chloroform should not be used as an anesthetic in cases where gas light is employed.

Besides its employment as an anesthetic by inhalation, chloroform is used internally as a sedative and externally as a rubefacient.

The official preparations of chloroform are the water (p. 199), the liniment (p. 291) and the spirit (p. 204).

Dose.—0.3 cc. (5 minims).

Bromoformum (U.S.P. IX) or *Bromoform* ($CHBr_3$) is made by treating alcohol or acetone with bromine in the presence of an alkali and distilling the bromoform resulting from the reacting liquid. Bromoform is a heavy transparent colorless mobile liquid having the specific gravity 2.595. It is recommended as a sedative, particularly in whooping cough, although its use for this purpose is not devoid of danger. *Dose.*—0.2 cc. (3 minims).

IODOFORMUM—Iodoform

(Iodof.)

CHI_3. Molecular weight, 393.77

Triiodomethane.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Fine lemon-yellow powder or hexagonal crystals; peculiar persistent odor; unpleasant sweetish taste; almost insoluble in water; soluble in about 48 parts of alcohol, in about 100 parts of glycerin, in about 15 parts of chloroform and in about 5.4 parts of ether; also soluble in carbon disulfide and olive oil; melts at 115° C. and volatilizes at higher temperatures. For details, see U.S.P., p. 195.

For *tests for identity* and for *impurities* (ash, soluble coloring matter, acids and alkalis), see U.S.P., p. 195.

Remarks.—Iodoform is a product chemically very similar to chloroform. Chloroform is trichlormethane; iodoform is tri-iodomethane. A graphic comparison may be useful:

$$\begin{array}{ccc} \text{Methane.} & \text{Chloroform.} & \text{Iodoform.} \\ (CH_4) & (CHCl_3) & (CHI_3) \\ \begin{array}{c} H \\ | \\ H-C-H \\ | \\ H \end{array} & \begin{array}{c} H \\ | \\ Cl-C-Cl \\ | \\ Cl \end{array} & \begin{array}{c} H \\ | \\ I-C-I \\ | \\ I \end{array} \end{array}$$

Iodoform is made by treating alcohol with the iodine in the presence of an alkali, the reaction being as follows:

$$\overset{\text{(Alcohol).}}{C_2H_5OH} + \overset{\text{Iodine.}}{I_8} = \overset{\text{Iodal.}}{CI_3CHO} + \overset{\text{Hydriodic acid.}}{5HI.}$$

$$\overset{\text{Iodal.}}{CI_3CHO} + \overset{\begin{array}{c}\text{Potassium}\\\text{hydroxide.}\end{array}}{KOH} = \overset{\text{Iodoform.}}{CHI_3} + \overset{\begin{array}{c}\text{Potassium}\\\text{formate.}\end{array}}{HCOOK.}$$

It will be seen in the above reaction that only 3 of the 8 atoms of iodine employed are converted into iodoform, the other five forming hydriodic acid. In view of the high cost of iodine such waste cannot be permitted, and, therefore, chlorine is passed through the reacting liquid, with the formation of HCl and liberation of iodine, the 5 atoms of which are in time converted into iodoform. In practice, potassium bicarbonate is the alkali employed in the above reaction. Iodoform is now largely made by electrolytic methods.

The manufacture of iodoform, by the way, affords an excellent test for alcohol, even when present in minute proportions. To the alcoholic liquid is added a grain or so of iodine and a few drops of solution of potassium hydroxide, and the mixture is gently warmed. If there settles out a yellow precipitate of the characteristic iodoform odor, the liquid contains alcohol.

Iodoform, which was discovered by Serullas in 1822, is one of the most valuable antiseptics, the sole objection to its use being its very disagreeable odor. Many efforts are noted in pharmaceutic journals for masking this odor, but none have proved satisfactory, about the most successful masker being coumarin.

The antiseptic properties of iodoform being due to iodine, several odorless iodine preparations have been put on the market as substitutes for iodoform. The most popular of these iodoform substitutes are *iodol* (p. 764) and *aristol* (p. 822), and neither of these can approach iodoform in actual percentage of iodine. Iodoform contains 96 per cent of iodine, as an estimation of the molecular weight will show, while iodol contains 84 per cent and aristol contains 46 per cent.

CARBONEI TETRACHLORIDUM—Carbon Tetrachloride

(Carb. Tetrachlor.)

CCl_4. Molecular weight, 153.83

Tetrachloromethane.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Clear, colorless, mobile liquid; characteristic odor; noninflammable; soluble in 2000 volumes of water: miscible with alcohol, chloroform, ether, benzene and petroleum benzin; dissolves fixed and volatile oils; sp. gr. 1.588 to 1.590; boils between 76° and 77° C. For details, see U.S.P., p. 109.

For *tests for identity* and for *impurities* (chloride, free chlorine, carbonizable substances, carbon disulfide), see U.S.P., p. 109.

Remarks.—This official has come into extended use during the last thirty years. It is made by passing the vapors of carbon disulfide and chlorine over a heated catalyst, such as metallic iron or ferric chloride.

It is a volatile liquid having the specific gravity 1.59 and its vapor is poisonous. It is used as a fire extinguisher, and as an ingredient for making benzin noninflammable. Its use in cleansing the hair should be prohibited, as death has resulted from its employment in that manner.

Of late years it has been used largely as a remedy for hookworm. (See p. 841.)

Dose.—Anthelmintic, for adults, single dose 2.5 cc. (40 minims).

Methyl alcohol (CH_3OH) was obtained by Robert Boyle in 1661 as a product in the destructive distillation of wood. By reason of its source its common name is *wood alcohol*, while a purer form of wood alcohol has been put on the market under the trade name of *methanol*.

Of theoretic interest is the manufacture of wood alcohol from methyl salicylate or oil of wintergreen, this product being treated with sodium hydroxide, yielding sodium salicylate and methyl hydroxide or wood alcohol (p. 801).

The commercial manufacture, however, is by the destructive distillation of wood. Wood cut into billets, placed in iron retorts, and heated, yields, besides gases, a tarry liquid called wood vinegar, or crude *pyroligneous acid*, which consists of a mixture of methyl alcohol, acetone, acetic acid, and a large number of other products. To the crude distillate, lime is added and the methyl alcohol and acetone are separated from the calcium acetate, thus formed, by a second distillation. The methyl alcohol and the acetone are then separated from each other by careful fractional distillation, although sometimes chemicals, such as calcium chloride, are used to accomplish the separation.

During 1925, large quantities of methyl alcohol (methanol) were imported into the United States from Germany and offered at prices considerably below the factory price of methanol made from wood, it being claimed that the cost of manufacture of the German methanol was between 18 and 26 cents a gallon. This German methanol is made synthetically and it is reported that the synthesis is based upon a French patent taken out by Patart (No. 540343) which covers the reaction between carbon monoxide and hydrogen, under pressure and in the presence of catalysts, the equation being:

$$CO + 2H_2 = CH_3OH.$$

While wood alcohol is a useful solvent, its toxic properties and its tendency to produce blindness, even when applied externally, has resulted in the prohibition of its use in medicinal and toilet preparations.

Methyl ether, $(CH_3)_2O$ is unofficial, and is mentioned only as the first representative of the class of ethers regarding which full explanation will be given when considering the official ether (p. 660).

Methyl ether is made by treating wood alcohol with sulfuric acid, and is popular in certain sections of Ireland as a tipple.

Methyl salicylate is the first representative of the official esters, and is official in three forms: (*a*) the synthetic methyl salicylate; (*b*) oil of wintergreen; and (*c*) oil of sweet birch, the two last mentioned being natural products, consisting chiefly of the chemical above mentioned. It is more convenient, however, to consider this substance under the head of salicylic acid, hence it is deferred until that time (p. 801).

Formaldehyde (HCHO), like all other aldehydes, is produced by the oxidation of the corresponding alcohol, which in this case is methyl alcohol; the reaction can be more clearly expressed as follows:

$$HCH_2OH + O = H_2O + HCHO.$$

The usual method of manufacture of aldehydes from the appropriate alcohols is by the oxidation with potassium dichromate and sulfuric acid, but in the case of formaldehyde oxidation by chemical means usually does not stop at formaldehyde, but is apt to produce formic acid or even to split into carbon dioxide and water; hence the oxidation of wood alcohol into formaldehyde is best accomplished without the aid of chemicals, and is usually performed by the incomplete combustion of methyl alcohol. If gaseous formaldehyde is desired, this combustion is accomplished by burning the formaldehyde from a wick and covering the flame with a cone of platinum wire. Such is the principle of most of the formaldehyde lamps now largely used for purposes of disinfection. The same results can be obtained by heating wood alcohol in a flask, and as the vapor begins to rise, immersing therein a red-hot platinum spiral. The commercial method of manufacture of the chemical is by passing the vapors of wood alcohol through heated tubes containing platinum or copper spirals or disks.

Formaldehyde is a gas of a peculiar pungent odor, and is placed on the market in aqueous solution, the commercial *formalin* being a 37 per cent (saturated) solution of same. This is now official as *liquor formaldehydi.*

Formaldehyde is a valuable antiseptic, hence the use of formaldehyde in lamps for the disinfecting of rooms. In room disinfection, the gas, HCHO, is liberated from its solution by addition of potassium permanganate, or potassium dichromate and sulfuric acid, or of chlorinated lime. While such room disinfection is carried out in crude containers, the chemicals must be mixed very carefully.

The use of formaldehyde solution as a food preservative is prohibited inasmuch as experiments have shown that formaldehyde, even in minute traces, injures digestion.

Formaldehyde forms with gelatinous substances insoluble compounds, and for this purpose is employed in solidifying glycerin jelly for microscopic mounts, and since hide is largely gelatin, formaldehyde can be employed for converting same into leather. The tests for formaldehyde are important in food analyses and in the examination of grain alcohol. Hehner's test is based on the violet color produced when minute quantities of ferric chloride, protein and formaldehyde are mixed, while in Leach's method of detecting formaldehyde in milk, hydrochloric acid containing some ferric chloride is added to the sample, which is then warmed, when a violet color indicates formaldehyde. Like all aldehydes and ketones, a formaldehyde solution restores the color of a fuchsin solution that has been bleached with sulfurous acid. This fact is made use of in the official test for wood alcohol in grain alcohol. (See p. 657.)

From formaldehyde many interesting syntheses have been made, the most striking of which was the condensing of same under treatment of calcium hydroxide into formose or acrose, a variety of sugar having the formula of $C_6H_{12}O_6$. This was accomplished by Lowe (1886), and gives an inkling of that wonderful method whereby plants, by the absorption of carbon dioxide from the air, grow from a seed to the large and lusty organism, the tree.

The entire details of the process are not yet fully understood, but it is generally accepted today that the conversion of carbon dioxide into other carbon compounds is accomplished chiefly by the intermediate product, formaldehyde.

Plants absorb carbon dioxide and water, and in these two bodies, CO_2 and H_2O, we have the elements that will form HCHO. The next step in the process has been accomplished in Loew's synthesis. Formaldehyde is CH_2O. If CH_2O is multiplied by six, the result is $C_6H_{12}O_6$. Theoretically, it seems simple to convert glucose, $C_6H_{12}O_6$, into sugar, $C_{12}H_{22}O_{11}$, as explained on p. 693, and likewise to convert sugar into starch, $C_6H_{10}O_5$, and into cellulose, which has the same proportional formula and which is the main constituent of woody tissue.

The conversions have not been practically accomplished, but it can be comprehended as plausible, since the reverse operation has been done. Cotton or starch treated with sulfuric acid will yield glucose.

To sum up the process by which plants grow:

H_2O and CO_2 should give HCHO, formaldehyde.
6HCHO does give $C_6H_{12}O_6$, acrose, a form of glucose.
$C_{12}H_{24}O_{12}(2C_6H_{12}O_6)—H_2O$ should give $C_{12}H_{22}O_{11}$, sugar.
$C_{12}H_{22}O_{11}—H_2O$ should give $C_{12}H_{20}O_{10}$ or $2C_6H_{10}O_5$.
$(C_6H_{10}O_5)$ is the formula of starch and cellulose.

Strassburger, after extensive microscopic and chemical work, decides that the method of starch formation in plants is not as simple as here outlined. He claims that very intricate intermediate products result, which is very likely, as nature rarely performs the synthesis in a direct manner. The above explanations are, therefore, merely approximate, their aim being to impress the wonderful manner in which plants live and increase on nutriment drawn almost exclusively from the air.

LIQUOR FORMALDEHYDI—Solution of Formaldehyde
(Liq. Formaldehyd.)

An aqueous solution containing not less than 37 per cent of CH_2O, with variable amounts of methanol to prevent polymerization.

Storage.—Preserve in a moderately warm place and protected from light.

Summarized Description.

Clear colorless liquid; pungent odor; caustic and irritating; miscible with alcohol and water; in cold and on standing becomes turbid (paraformaldehyde precipitates). For details, see U.S.P., p. 210.

For *tests for identity* and for *impurities* (free acid) and for *assay*, see U.S.P., p. 210.

Remarks.—In view of the full statements as to formaldehyde given on page 649, further comments are not necessary.

Paraformaldehydum (U.S.P. X), or *Paraformaldehyde*, or *Trioxymethylene*, contains not less than 95 per cent of $(HCHO)_3$. It represents a polymer of formaldehyde in which 3 molecules of HCHO are condensed into one molecule. The condensation can be accomplished by the simple expedient of cautiously evaporating the official solution of formaldehyde.

It is a white crystalline powder, that is used as an antiseptic and escharotic.

Sodium formaldehyde sulfoxylate, $HCHO—NaHSO_2—H_2O$ has been used for a number of years as an antichlor in the textile industry. Latterly it has been recommended as an antidote for mercuric chloride. (See p. 616.)

Acidum Formicum or *Formic Acid*, HCOOH, was discovered by Fischer and Ray in 1670, they finding same in the distillate from red ants (*Formica rufa*), hence the name. Formic acid is likewise a constituent of the hairs of the stinging nettle, *Urtica dioica*. Whether the poisonous effect of the sting of the ant and of the nettle is due to the formic acid or to a toxic enzyme is still an unsettled question.

Potassium cyanide on being cooked yields potassium formate. This, however, is not commercial method of manufacture, and is merely suggested as a warning that pharmacists should never use heat in preparing solutions of potassium cyanide. While formic acid can be made by oxidation of methyl alcohol, it is usually prepared by heating oxalic acid with glycerin, the distillate being practically pure formic acid. It is also made synthetically from carbon dioxide and hydrogen by use of heat, pressure and the suitable catalyst (palladium).

Formic acid is a reducing agent, being capable of producing the separation of metallic silver from the solution of silver nitrate. It is the only acid of the series possessing reducing power.

Formamide, $HCONH_2$, produced by the condensation of formic acid with ammonia, is the basis of several synthetic medicines. (See p. 667.)

The Methylamines.—Of these, the only one of pharmaceutic value is *trimethylamine*, $(CH_3)_3N$. This body was introduced into the market under the name of *propylamine*, it being an isomere of that body which has the formula of $C_3H_7NH_2$. It is found in small traces in arnica root, and in the brine used for pickling herring. Its commercial source is beet sugar residues, and it had considerable vogue for rheumatism, but its disagreeable taste prevented its general use. Dose, 2 to 4 drops.

BIBLIOGRAPHY

Hydrocarbons.—Perry, Jl. Am. Ch. Soc., 54, 1932, 2918.

Alcohols.—Couch, A.J.P., 95, 1923, 533; Danner and Hillebrand, Jl. Am. Ch. Soc., 44, 1922, 2824 and 2832; Williams and Truesdail, *ibid.*, 45, 1923, 1348; Lucas, *ibid.*, 52, 1930, 802; Henze and Blair, *ibid.*, 53, 1931, 3042; Stewart and Edwards, C.A., 26, 1932, 1168.

Esters.—Sadtler, A.J.P., 95, 1923, 284.

Radicals.—Gomberg, Jl. Ind. Eng. Ch., 6, 1914, 339; 20, 1928, 159; Paneth and Hofeditz, Jl. Soc. Ch. Ind., 48, 1929, 1015; Paneth and Lautsch, C.A., 24, 1930, 3750; Pearson and co-workers, C.A., 26, 1932, 4299.

Amines.—Meyer and Sicco, A., 180, 1875, 176; Hager and Marvel, Jl. Am. Ch. Soc., 48, 1926, 2689.

Methane.—Henri, C.A., 21, 1927, 3886; Randall and Gerard, Jl. Ind. Eng. Ch., 20, 1928, 1335; Brindley, C.A., 23, 1929, 3398; Mooy, C.A., 25, 1931, 3891; Storch, C.A., 26, 1932, 2361.

Natural Gas.—Tanasecu, C.A., 7, 1913, 2295; Burrell and Seibert, Jl. Am. Ch. Soc., 37, 1915, 396; Anon., Jl. Soc. Ch. Ind., 41, 1922, 525R, Hirschi, C.A., 8, 1914, 816; Wilson, Jl. Ind. Eng. Ch., 18, 1926, 1273; Robertson, *ibid.*, 22, 1930, 1268; Hopkins, *ibid.*, 22, 1930, 502; Allen, Jl. Soc. Ch. Ind., 49, 1930, 274.

Petroleum.—(Source and origin) Ipatiev, C.A., 6, 1912, 678; Breger, C.A., 6, 1912, 678; Anon., C.A., 5, 1911, 3728; Anon., C.A., 5, 1911, 2472; Holde, Jl. Ind. Eng. Ch., 6, 1914, 35; Mabery, Jl. Ind. Eng. Ch., 6, 1914, 101 and Jl. Am. Ch. Soc., 41, 1919, 1690; Kizhner, C.A., 9, 1915, 2147; Pictet and Potok, Dr. Circ., 64, 1920, 180; Anon., Jl. Soc. Ch. Ind., 42, 1923, 689; Le Bel, C.A., 22, 1928, 3606; von Stahl, C.A., 26, 1932, 5881. (Production) Anon., Ch. News, 117, 1918, 28 and 211; Shotwell, Jl. Soc. Ch. Ind., 42, 1923, 1028; Burrell, C.A., 14, 1920, 835; Anon., Jl. Soc. Ch. Ind., 39, 1920, 107R; Nathan, *ibid.*, 46, 1927, 211T; Anon., *ibid.*, 50, 1931, 958; Anon., *ibid.*, 51, 1932, 838; Anon., Jl. Frank. Inst., 202, 1926, 546A; Elin, J. Soc. Ch. Ind., 47, 1928, 989. (History) Redwood, Jl. Soc. Ch. Ind., 27, 1908, 779; Johns, Jl. Ind. Eng. Ch., 15, 1923, 446; Raubenheimer, Dr. Circ., 54, 1910, 621; Stroup, A.J.P., 102, 1930, 631. (Cracking) Johns, see above; Lomax, Dunstan and Thole, Jl. Ind. Eng. Ch., 9, 1917; 879; Nakagawa, C.A., 14, 1920, 219. (Classification) Holde, C.A., 6, 1912, 1983.

Benzin.—Raubenheimer, Dr. Circ., 52, 1908, 421.

Gasoline.—Hosmer and Seibert, Jl. Ind. Eng. Ch., 14, 1922, 1106; Robson and Withrow, C.A., 13, 1919, 2437; Oberfell and co-workers, C.A., 13, 1929, 4055.

Liquid Petroleum.—(Composition) Krajenski, C.A., 5, 1911, 3620; Vicario, C.A., 8, 1914, 2601; Brooks, Jl. A.M.A., 66, 1916, 24 and 38. (Properties) Gane, Jl. A.Ph.A., 4, 1915, 792; Peck, Ph. Jl., 92, 1914, 28 and 508; Flescher, Drug Trade News, 51, Feb. 18, 1935, reprint; Meyer, Jl. A.Ph.A., 24, 1935, 319. (Uses) Hilton, Jl. A.Ph.A., 3, 1914, 577; Wilbert, A.J.P., 86, 1914, 150; Bastedo, J.A.M.A., 64, 1915, 808; Remington, Proc. P.P.A., 38, 1915, 230; Gane, A.J.P., 87, 1915, 792; Humphreys, J. A.Ph.A., 5, 1916, 304; Wood, A.J.P., 102, 1930, 342; Parsons, Ph. Jl., 129, 1932, 112.

Petrolatum.—(History and manufacture) Miller, A.J.P., 46, 1874, 4; Stacey, A.Ph.A., 23, 1875, 630. (Composition) Mabery, Am. Acad. Arts. Sci., 40, 1904, 340 and 361.

Petrox Preparations.—Wilbert, A.J.P., 73, 1901, 220; Beringer, A.J.P., 83, 1911, 243.

Paraffin.—(History) Crooks, 44, 1925, 599. (Manufacture and properties) Stacey, A.Ph.A., 23, 1875, 629; Morris and Adkins, *ibid.*, 19, 1927, 301. (Composition) Pawlewski, B., 23, 1890, 327; Ferris and co-workers, Jl. Ind. Eng. Ch., 21, 1929, 1092. (Uses) Rossman, C.A., 24, 1930, 1506.

Ceresin.—Shotsky, Am. Dr., 19, 1890, 173.

Chlorcosan.—Dakin and Dunham, Ch. and Dr., 90, 1918, 73; Harris, Jl. A.Ph.A., 9, 1920, 39; Cook, Proc. A.J.Ph.A., 48, 1918, 41.

Ichthyol.—(History) Anon., Ch. and Dr., 89, 1917, 210. (Composition) Hayek, A.Ph.A., 56, 1908, 305; Beckurts and Frerichs, Arch. de. Pharm., 250, 1912, 478; Passmore, Yearbook, A.Ph.A., 1, 1912, 318; Anon., Jl. A.M.A., 72, 1919, 345; Thompson, Proc. N. Y. S.P.A., 42, 1920, 198. (Miscibility) Hostmann, Jl. A.Ph.A., 4, 1915, 1490.

Methyl Chloride.—(Manufacture) Groves, Jl. Ch. Soc., 27, 1874, 641; Vincent, J. B., 2, 1878, 1134. (Uses) Kegel and co-workers, Jl. A.M.A., 93, 1929, 353; Yant and co-workers, C.A., 24, 1930, 4561.

Chloroform.—(History) Guthrie, West. Dr., 16, 1894, 57; Davis, Merck's Rep., 39, 1930, 153; Speter, Ph. Zent., 72, 1931, 628; Dobbin, Ch. and Dr., 115, 1931, 761; Gilmour, *ibid.*, 133, 1934, 75. (Structure) Dumas, A., 16, 1835, 164. (Manufacture) Dott, Ch. and Dr., 72, 1908, 299; Frerichs, Jl. Ind. Eng. Ch., 4, 1912, 346 and 406; Dott, Jl. Soc. Ch. Ind., 27, 1908, 271; Squibb, Jl. Am. Ch. Soc., 18, 1896, 237; Feyer, Jl. Soc. Ch. Ind., 38, 1919, 599A; Lowy, Jl. Ind. Eng. Ch., 15, 1923, 15. (Purification) Pictet, Jl. Soc. Ch. Ind., 11, 1892, 59. (Properties and tests) Squibb, A.J.P., 29, 1857, 430; Hofmann, B., 3, 769; Schrool and Van den Berg, B. ph. Ges., 15, 1905, 387; Iterson and Fischer, Ph. Zt., 34, 1889, 221. (Preservation) Sadtler, A.J.P., 95, 1923, 273; Oberhard, Jl. Soc. Ch. Ind., 48, 1929, 338B. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1153; Hill, Jl. Am. Ch. Soc., 54, 1932, 32. (Uses and action) Anon., Nat. Dr., 39, 1909, 209; Nicloux, Comp. rend., 150, 1910, 1777; Clover, Jl. Am. Ch. Soc., 45, 1923, 3133.

Anesthesia.—(Discovery) Jacobs, A.Ph.A., 45, 1897, 315 and Jl. A.Ph.A., 13, 1924, 51.

Bromoform.—Guenther, Am. Dr., 16, 1887, 204; Buhmann, Arch. d. Pharm., 266, 1928, 123.

Iodoform.—(History) Engelhardt, Am. Dr., 55, 1909, 73. (Manufacture) Caspari, A.Ph.A., 54, 1906, 326; Lieben, Am. Dr., 19, 1890, 173. (Properties) Lafforg, Meyer Bros. Drug, 31, 1910, 105.

Carbon Tetrachloride.—(Manufacture) Anon., Am. Dr., 55, 1909, 9; Sadtler, A.J.P., 95, 1923, 280. (Uses) Robinson, C.A., 5, 1911, 233; Raubenheimer, A.Ph.A., 51, 1903, 426; Waller, C.A., 3, 1909, 584; Hall, C.A., 15, 1921, 2499; Warren, A.J.P., 95, 1923, 864; Docherty, C.A., 7, 1924, 124; Caius and Mhaskar, C.A., 18, 1924, 1338 and 1529; Anon., Jl. Soc. Ind., 44, 1925, 31B; Ormandy, *ibid.*, 46, 1927, 483. (Pharmacology and toxicology) Leach and co-workers, C.A., 18, 1924, 865; Phelps and Hu, Jl. A.M.A., 82, 1924, 1254; Fülleborn, C.A., 19, 1925, 539; Rawson, C.A., 26, 1932, 3576.

Methyl Alcohol.—(History) Vogel, Ch. Zt., 32, 1908, 651; Anon., Jl. Ind. Eng. Ch., 19, 1927, 227. (Manufacture) Hawley and Palmer, Bull. U. S. Dept. Agr., No. 129. French and Withrow, Jl. Ind. Eng. Ch., 7, 1915, 47; Greer, Forest Service Bull. U. S, Dept. Agr., No. 114; Palmer, Jl. Ind. Eng. Ch., 7, 1915, 663; Anon., C.A., 16, 1922; 2986; Hunt, A.J.P., 97, 1925, 495; Carlin, A.J.P., 102, 1930, 132. (Synthesis) Patart, Jl. Soc. Ch. Ind., 44, 1925, 83B, 336B and 882; Fischer, Jl. Ind. Eng. Ch., 17, 1925, 574; Anon., *ibid.*, 17, 1925, 981; Lormand, *ibid.*, 17, 1925, 430; Valette, C.A., 22, 1928, 4461; Brown and Galloway, Jl. Ind. Eng. Ch., 20, 1928, 960; 21, 1929, 310 and 22, 1930,

175; Audibert and Raineu, *ibid.*, 20, 1928, 1105; Audibert, C.A., 23, 1929, 1385 and Jl. Soc. Ch. Ind., 48, 1929, 162B; Storch, *ibid.*, 47, 1928, 885B; Johnson, *ibid.*, 48, 1929, 549B; Kelly, Jl. Ind. Eng. Ch., 21, 1929, 310; Cryder and Frolich, *ibid.*, 21, 1929, 867; Frolich, *ibid.*, 23, 1931, 111; Taylor, Jl. Soc. Ch. Ind., 50, 1931, 317; Morgan, *ibid.*, 49, 1930, 742; 50, 1931, 104 and 51, 1932, 3T. (Uses and dangers) Baskerville, Jl. Ind. Eng. Ch., 5, 1913, 768; Loewy, Jl. A.M.A., 63, 1914, 915; Tyson and Schoenberg, Jl. A.M.A., 63, 1914, 915; Yant and Sayers, Jl. Ind. Eng. Ch., News Ed., 8, 1930, 4 and Jl. Ind. Eng. Ch., 23, 1931, 551; McCord, *ibid.*, 23, 1931, 931. (Tests) Whaley, Jl. Ind. Eng. Ch., 20, 1928, 320; Leffmann and Pines, A.J.P., 101, 1929, 584.

Methyl Ether.—Anon., Am. Dr., 19, 1890, 226; Edit., Ch. and Dr., 107, 1927, 577.

Formaldehyde.—(History and source) Moore and Webster, Jl. A.M.A., 61, 1913, 2305; Curtius and Franzen, B., 45, 1912, 1715; Schryver, A.Ph.A., 58, 1910, 322. (History and manufacture) Hofmann, Ch. News, 17, 1868, 63 and 82; Tollens and Mayer, B., 21, 1888, 3507; Vorisek, Jl. Soc. Ch. Ind., 28, 1909, 823; Tollens, Jl. Soc. Ch. Ind., 15, 1896, 290; Thomas, Jl. Am. Ch. Soc., 42, 1920, 867; Berger, C.A., 16, 1922, 3355; Bobrov, C.A., 18, 1924, 1467 and 19, 1925, 465; Schwyzer, Ph. Zt., 75, 1930, 28 and 45. (Synthesis) Armstrong, Jl. Soc. Ch. Ind., 49, 1931, 178. (Properties and uses) Bird, Ph. Jl., 57, 1896, 269. (Tests) Hehner, Leonard, Analyst, 21, 1896, 157. (Disinfection with) Base, A.Ph.A., 55, 1907, 896; LaWall, Jl. A.M.A., 63, 1914, 1025; Williams, Jl. A.Ph.A., 5, 1916, 185; Horn and Osol, A.J.P., 101, 1929, 741; Horn and Hunter, *ibid.*, 103, 1931, 332. (Condensations) Tollens, Jl. Ch. Soc., 46, 1884, 293; Loew, Jl. prakt. Ch., 33, 1886, 321; Borkorny, C.A., 6, 1912, 241; Strassburger, Times' Lectures, 1886, 180; Rosenthaler, Arch. Pharm., 251, 1913, 587; Raikow, C.A., 9, 1915, 3086; Ewart, *ibid.*, 13, 1919, 1083; Baly and Heilbron, Jl. Soc. Ch. Ind.. 40, 1921, 377R.; Spoehr and Sheppard, Jl. Soc. Ch. Ind., 42, 1923, 99; Sabalitschka, *ibid.*, 42, 1923, 65A; Loew, C.A., 19, 1925, 2473; Baly, Jl. Ind. Eng. Ch., 16, 1924, 1016, Cattelain, Jl. de ph. et ch., [8], 9, 1929, 70, 113 and 153.

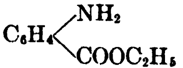
Formic Acid.—(History) Chattaway, Ch. News, 109, 1914, 61. (Sources) Gorup-Besanez, A.J.P., 22, 1850, 181; Gaillard, A.J.P., 50, 1878, 116; Haberlandt, A.J.P., 58, 1886, 252; Berger, Schw. Ap. Zt., 50, 1912, 51 and 72; Sumpter, C.A., 17, 1923, 153; Dobbion, Ph. Jl., 103, 1919, 321; Tschirch, Dr. Circ., 64, 1920, 257; Flury, C.A., 22, 1928, 4149; De Vasconcelles, C.A., 25, 1931, 1592. (Properties) Garner Saxton and Parker, Jl. Am. Ch. Soc., 46, 1924, 236. (Manufacture) Fell, A.J.P., 30, 1850, 218; Berthelot, A.J.P., 28, 1856, 557. (Synthesis) Bredig and Carter, Jl. Soc. Ch. Ind., 49, 1930, 235.

Formates.—Luman, A.Ph.A., 57, 1909, 363.

CHAPTER XXXVII

ETHANE DERIVATIVES

THE derivatives of ethane of pharmaceutic value are:

Ethylene, U.S.P.		$CH_2{:}CH_2$.
Ethyl chloride, U.S.P.		C_2H_5Cl.
Alcohol, U.S.P.		C_2H_5OH.
Whisky, U.S.P.	(containing 47 to 53 per cent	C_2H_5OH).
Brandy, U.S.P.	(containing 48 to 54 per cent	C_2H_5OH).
Ether, U.S.P.		$(C_2H_5)_2O$.
Ethyl oxide		$(C_2H_5)_2O$.
Ethyl sulfate		$(C_2H_5)_2SO_4$.
Ethyl nitrite		$C_2H_5NO_2$.
	(in spirit of ethyl nitrite, U.S.P.)	
Ethyl aminobenzoate		 $C_6H_4\begin{cases}NH_2\\COOC_2H_5\end{cases}$
	(described among the benzoic acid derivatives)	
Ethyl acetate		$C_2H_5C_2H_3O_2$.
Ethyl chaulmoograte		
	(described under chaulmoogra oil)	
Aldehyde		CH_3CHO.
Paraldehyde, U.S.P.		$(CH_3CHO)_3$.
Chloral hydrate, U.S.P.		$CCl_3CHO + H_2O$.
Acetic acid, U.S.P.		CH_3COOH.
Sodium cacodylate, U.S.P.		$Na(CH_3)_2AsO_2$.
Trichloracetic acid, U.S.P.		CCl_3COOH.
Oxalic acid		$(COOH)_2$.

ÆTHYLIS CHLORIDUM—Ethyl Chloride

(Æthyl. Chlor.)

C_2H_5Cl. $CH_3.CH_2.Cl$. Molecular weight, 64.50

Monochlorethane.

Storage.—Preserve in hermetically sealed containers, in a cool place, remote from fire and protected from light.

Summarized Description.

Colorless, mobile, very volatile liquid at low temperatures or under pressure; boils between 12° and 13° C.; vapor very inflammable; burns with a smoky greenish flame producing hydrogen chloride. For details, see U.S.P., p. 42.

For *tests for identity* and for *impurities* (ionized chloride, alcohol), see U.S.P., p. 42.

Remarks.—Ethyl chloride is made by treating alcohol with hydrochloric acid gas. It can also be made, as already explained, as all other halogen derivatives of the hydrocarbons, by treatment of the appropriate hydrocarbon (in this case, ethane) with the proper halogen (in this case, chlorine).

Ethyl chloride is so volatile that it can be kept in its liquid form only when under heavy pressure in sealed glass tubes or metallic cylinders. Note that the vapor is inflammable and must be kept away from a flame. It is used, under such trade names as *kelene*, as a local anesthetic (as described under Rhigolene, p. 641), and is now being employed either by itself or in combination with chloroform or ether as a general anesthetic.

ÆTHYLENUM—Ethylene

(Æthylen.)

C_2H_4. $CH_2{=}CH_2$. Molecular weight, 28.03

Ethylene contains not less than 99 per cent by volume of C_2H_4. For convenience it is usually furnished in compressed form in metallic cylinders.

Caution.—Ethylene is inflammable, and its mixture with oxygen or air will explode when brought in contact with a flame or an electric spark.

Storage.—Preserve in well-closed containers, in a cool place, remote from fire and with ample ventilation to the outer air.

Summarized Description.

Colorless gas; sweet odor and taste; soluble in 4 volumes of water at 0° C., in 9 volumes of water at 25° C.; slightly soluble in alcohol and in ether. For details, see U.S.P., p. 38.

For *tests for identity*, for *impurities* (carbon dioxide, acetylene, aldehyde, hydrogen sulfide, phosphine, and carbon monoxide) and for *assay*, see U.S.P., p. 38.

Remarks.—Ethylene, C_2H_4, is made industrially by passing the vapors of ethyl alcohol over the proper catalyst, heated to the proper temperature. It is a colorless gas having a sweet odor and is used for the rapid ripening of certain fruit. When carefully purified, it has been found of value as an anesthetic.

Ethylene Dichloride, $C_2H_4Cl_2$, is a colorless liquid, smelling somewhat like chloroform. It is used as a solvent and as a moth and weevil killer.

Tetrachlorethylenum (N.F. VI), or *Tetrachlorethylene*, or *carbon dichloride*, $CCl_2{=}CCl_2$, is now used as an anthelmintic in veterinary medicine.

It is a clear, colorless, mobile liquid which is almost insoluble in water but which is miscible with alcohol, ether, chloroform, benzene and petroleum benzin. *Dose.*—3 cc. (45 minims).

Dichlorethylene, $C_2H_2Cl_2$, and other chlorinated compounds of ethane and ethylene, such as C_2HCl_3, C_2Cl_4, $C_2H_2Cl_4$ and C_2HCl_5, are now in considerable use as noninflammable, nonexplosive solvents. Dichlorethylene has been recommended as a solvent for iodine; "I.D.E." being a 2.48 per cent solution of iodine in that solvent.

Ethyl Hydroxide (C_2H_5OH) has been known from the earliest times in the form of alcoholic liquids, one of the first references being the well-known story of Noah and his vineyard.

The isolation was first performed by Salernus (twelfth century), and the name alcohol was first applied in the thirteenth century, the name being of Arabic origin.

Passing over the several syntheses of alcohol, it may be said that most commercial alcohol is made by the fermentation of substances containing starch or sugar. If dilute watery preparations of starch and sugar are allowed to stand, the spores of the yeast plant, *Saccharomyces cerevisiæ*, present in the air, locate in same and begin to grow, the process of the plant's assimilation producing in saccharine liquid the chemical change called *fermentation.* It was formerly considered that the chemical change could be produced only by the actual process of plant life, but it is now known that the fermentation is entirely due to the chemical action of the enzymes found in the protoplasm of yeast. The reaction of the fermentation expressed in simplest form is as follows:

$$C_6H_{12}O_6 = 2C_2H_5OH + 2CO_2,$$

but the real process is far more complicated, as is evidenced by the large number of side products of fermentation, such as glycerin, succinic acid, and amylic alcohols (fusel oil), invariably found in the fermented liquid. In order to obtain alcohol it is necessary to subject the fermented liquid (usually called the *mash*) to distillation. Commercial alcohol is now largely made by fermentation of molasses and distillation of the mash. Modern bakeries now have ovens which provide for the recovery of the alcohol from the fermentation process in making bread dough.

Of late years, alcohol has been made from sawdust, by converting the cellulose thereof into glucose by action of sulfurous acid or of a mixture of hydrochloric acid and zinc chloride under pressure and subsequent fermentation of the glucose thus produced.

Other methods, such as production of acetylene from calcium carbide and then bringing about a reaction between the acetylene and water by use of a catalyst, have been operated with some success.

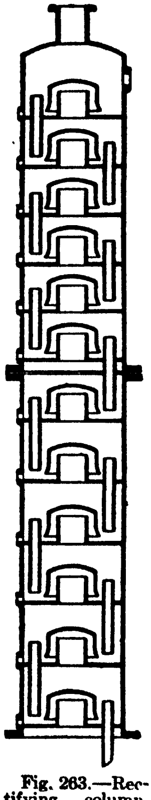


Fig. 263.—Rectifying column. Longitudinal section.

Alcohol or *ethanol* is obtained by the redistillation of whisky, the fusel oil, glycerin, and other extraneous matter being separated from same by the process called *dephlegmation.* This long word has been bequeathed us by the alchemists, whose favorite treatment of a substance was to submit it to distillation. If a portion thereof was volatile, the same was called *spirit,* while the less volatile portion which was left behind was called *phlegm.* To produce this spirit (alcohol) it was necessary to remove same from the phlegm and the process was called dephlegmation. This is accomplished by heating the whisky or the mash in an appropriate still body, and making the vapors rise through a tall tower or column before diverting same into the condensing worm. This tower or column apparatus is generally provided with a series of perforated disks which condense the less volatile portions, permitting the passage of pure alcohol vapors only. Figure 263 shows the longitudinal section of the rectifying column; Fig. 264 shows the entire rectifying still; while Fig. 265 shows a glass dephlegmator for smaller operations of the laboratory.

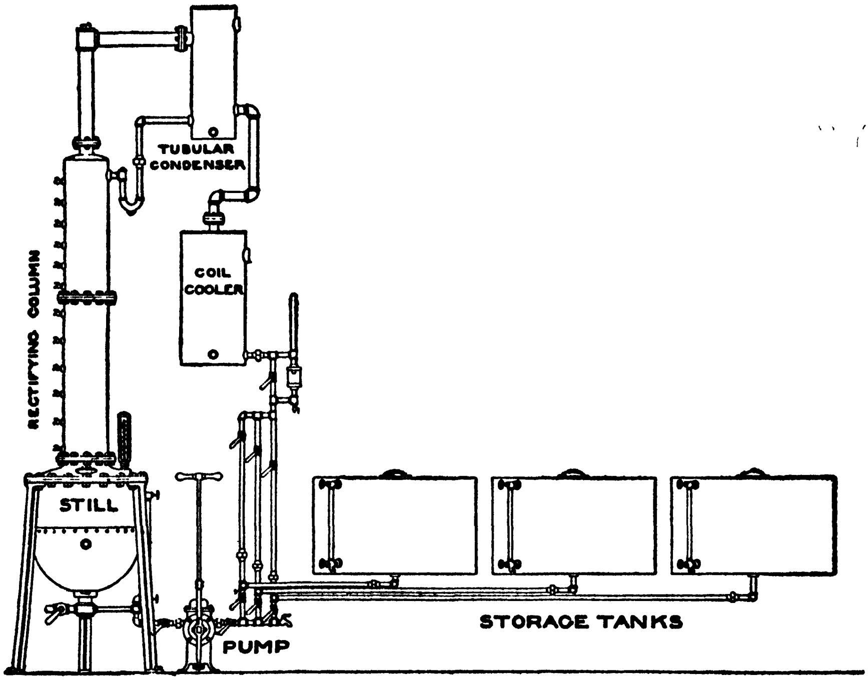


Fig. 264.—Rectifying still, with column and condensers.

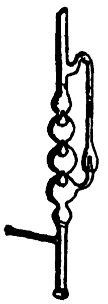


Fig. 265.—Glass dephlegmator.

ALCOHOL—Alcohol

(Ethanol, Ethyl Alcohol, Spiritus Vini Rectificatus)

C_2H_6O. $CH_3.CH_2OH$. Molecular weight, 46.05

A liquid containing not less than 92.3 per cent by weight, corresponding to 94.9 per cent by volume, at 15.56° C., of C_2H_5OH.

Storage.—Preserve in well-closed containers, in a cool place, remote from fire.

Summarized Description.

Colorless, mobile, volatile liquid; characteristic odor; burning taste; miscible with water, ether and chloroform; sp. gr. 0.816 at 60° F. and 0.810 at 25° C.; boils at 7°° C.; burns with a blue flame. For details, see U.S.P., p. 45.

For *tests for identity* and for *impurities* (fusel oil, amyl alcohol, aldehyde, organic impurities, methanol, acetone and denaturants), see U.S.P., p. 45.

Remarks.—This represents the most concentrated form of ethyl hydroxide which can be produced by the simple process of dephlegmation. It contains 92.3 per cent, by weight (94.9 per cent, by volume), of ethyl hydroxide and is practically the *deodorized alcohol* of the Pharmacopœia of 1890.

It is very important to be able readily to determine the strength of any individual sample of alcohol on hand, and this is usually accomplished by means of that form of hydrometer called the alcoholometer (already described on p. 62), which is usually provided with a scale which not merely reads its specific gravity, but also the actual percentage of alcohol in the sample. Of course, the strength can be ascertained by taking the specific gravity in any other manner, in which event, however, reference must be had to the alcohol table found in the Pharmacopœia.

It will be noticed that the pharmacopœial monograph includes a test for wood alcohol. This is based upon the fact that grain alcohol treated with a dilute acidulated permanganate solution does not oxidize to aldehyde, while wood alcohol so treated yields formaldehyde. The fuchsin-sulfurous acid reaction given in the test shows the presence of formaldehyde. (See p. 650.)

ALCOHOL DEHYDRATUM—Dehydrated Alcohol

(Alcohol Dehyd.—Dehydrated Ethanol, "Absolute Alcohol")

A liquid containing not less than 99 per cent by weight of C_2H_5OH.

Storage.—Preserve in well-closed containers, in a cool place, remote from fire.

Summarized Description.

Colorless, mobile, volatile liquid; characteristic odor; burning taste; very hygroscopic; sp. gr., 0.798 at 60° F. or 0.790 at 25° C.; otherwise like alcohol. For details, see U.S.P., p. 46.

For *tests for identity*, and for *impurities*, see Alcohol.

Remarks.—Dehydrated alcohol, or *absolute alcohol,* is a liquid containing not less than 99 per cent of ethyl hydroxide, and is made from ordinary alcohol by redistillation from lime. In order to get same "absolutely absolute," which is sometimes necessary in very careful chemical work, it is mixed with metallic sodium, which absorbs all the water (forming sodium hydroxide), and also some of the alcohol (forming sodium alcoholate, C_2H_5ONa), and then distilling into a flask closely fitted to the condenser, and with orifices for air closed by means of calcium chloride drying tubes.

Absolute alcohol is now made in large commercial quantities by the fractional distillate of a mixture of alcohol, water and a third component (called "entrainer" or "ternary agent") in a column still. Among the "ternary agents" may be cited benzene, toluene, carbon tetrachloride and ethyl acetate.

To tell whether absolute alcohol is completely dehydrated there is thrown into same a small amount of exsiccated copper sulfate. This is of grayish-white color, and if there is any water in the alcohol, the copper salt absorbs same, becoming partly crystallized, and assuming a blue tint.

ALCOHOL DILUTUM—Diluted Alcohol

(Alcohol Dil.—Diluted Ethanol)

A mixture of alcohol and water containing not less than 41 per cent and not more than 42 per cent by weight, corresponding to not less than 48.4 per cent and not more than 49.5 per cent by volume, at 15.56° C., of C_2H_5OH.

Storage.—Preserve in well-closed containers, in a cool place, remote from fire.

Condensed Recipe.

Mix together 500 cc. of alcohol and 500 cc. of distilled water; at 25° C. the product will measure about 970 cc.

Summarized Description.

Responds to reactions and tests given under alcohol; however, its specific gravity is from 0.935 to 0.937 at 60° F. or 0.930 to 0.932 at 25° C. For details, see U.S.P., p. 47.

Remarks.—Diluted alcohol, U.S.P., is made by mixing equal volumes of alcohol and water, and since U.S.P. alcohol is 92.3 per cent, by weight, of ethyl hydroxide, the dilute alcohol is 41 per cent, by weight, of the same chemical. This is shown in the following figures:

100 cc. of 92.3 per cent alcohol (sp. gr. 0.820) weighs 82 Gm.

100 cc. or 82 Gm. 92.3 per cent alcohol
plus 100 cc. or 100 Gm. water
makes 200 cc. or 182 Gm. of diluted alcohol.
The 82 Gm. 92.3 per cent alcohol contain 92.3 Gm. absolute alcohol.
$(82 \times 0.923 = 75.68)$.
Hence the 182 Gm. diluted alcohol contain the same—
75.68 Gm. absolute alcohol.
What percentage of 182 is 75.68?

$$\frac{75.68}{182.00} \times 100 \text{ per cent, or about } 41.5 \text{ per cent.}$$

Note that 100 cc. alcohol and 100 cc. water do not make 200 cc. diluted alcohol, and this variation from the theoretic is due to the interesting fact that when alcohol and water are mixed, contraction occurs, as explained on p. 145.

It is important to know that diluted alcohol, U.S.P., is not the "proof spirit" of the Internal Revenue Department of the government; the latter means 50 per cent by volume of ethyl hydroxide, while the dilute alcohol, U.S.P., is from 48.4 to 49.5 per cent by volume. As is usual with commercial standards, the Internal Revenue grading is wholly unscientific.

In choosing 50 per cent by volume as "proof," possibly a correct standard was made, as it is assumed that most whisky is about that strength. However, the strength, either above or below this point, is designated in a most unfortunate manner, viz., by saying that sample is "ten below proof" or "twenty above proof." Twenty above proof does not mean 70 per cent by volume, but indicates that 100 parts of such 20 above proof sample are to be diluted with water enough to make 120 parts in order to make it "proof." In other words, "20 above proof" means 60 per cent by volume.

Still more unfortunate is it that British excise "proof" is not the same as the standard of the Internal Revenue of our country, but represents 50 per cent, by weight, of absolute alcohol.

Denatured Alcohol represents commercial ethyl alcohol made unfit for beverage purposes by addition of chemicals of disagreeable taste which cannot be removed from the alcohol by distillation or by addition of chemicals. The original denaturing formula used by the American authorities consisted of alcohol, methyl alcohol (9 per cent) and kerosene (0.5 per cent). Five denaturing formulas are now in use for alcohol intended for general sale and 53 formulas are permitted for specific cases of manufacturing. Such denatured alcohol is free from the Internal Revenue tax.

ALCOHOLIC LIQUORS

Since ancient times various forms of alcoholic liquors have been used for beverage purposes. During the period 1920 to 1933 when the Eighteenth Amendment was in force the use of such alcoholic liquors for beverage purposes was legally taboo. As the medicinal use of certain of these beverages is important, a brief description of the more popular of these is worthy of a space in this book.

Wines are made by the fermentation of the juice of grapes and eventual clarification of the same. **Vinum Album** (U.S.P. VIII) or *White Wine* is made by fermenting the juice of the grape, freed from the skins; while **Vinum Rubrum** (U.S.P. VIII) or *Red Wine* is obtained by the fermentation of the juice of the red grapes in the presence of the skins.

Champagne deserves passing comment. This represents white wine containing from 8 to 9 per cent of alcohol, carbonated with carbon dioxide generated during the process of fermentation. The sweetened wine with a minute quantity of yeast is placed in tightly stoppered bottles, which are inverted on a rack and left in a room, the temperature of which favors fermentation. When the fermentation has reached the proper stage—which is determined by experience—the wine is left to cool for several months, during which time the sediment collects in the neck of the bottle while the gas collects at the inverted bottom. When completely settled, an expert workman passes from bottle to bottle, drawing out the corks for a period long enough to remove the sediment without serious loss of the other contents. The product is then corked securely and sent to market. It can readily be seen that the operation of removing the sediment is exceedingly delicate, and can be accomplished only with loss of quantities of the contents of a large number of bottles. This loss plus the loss of breakage of bottles during process of fermentation gives the real reason for the high cost of champagne.

Beer.—This is the product of the fermentation of malt, hops being added to give the product a characteristic taste. The ordinary lager beer contains 3 to 4 per cent of alcohol; the dark, heavy Munich beer contains 8 per cent of alcohol, while the so-called "Berlin" or Weiss beer contains only 2 per cent, which amount is too small to effect complete preservation of the product, hence it must be fresh when dispensed.

SPIRITUS FRUMENTI—Whisky

(Sp. Frum.)

An alcoholic liquid obtained by the distillation of the fermented mash of wholly or partly malted cereal grains, and containing, at 15.56° C., not less than 47 per cent and not more than 53 per cent, by volume, of C_2H_5OH. It must have been stored in charred wood containers for a period of not less than four years.

Summarized Description.

Amber-colored liquid; characteristic odor and taste; sp. gr. 0.935 to 0.923. For details, see U.S.P., p. 355.

For *tests for identity* and for *impurities* (acetone, methanol, alkaloids, caramel, formaldehyde, glycerin, sugar, heavy metals, isopropyl alcohol, esters, tertiary butyl alcohol), see U.S.P., p. 355.

Remarks.—Whisky is the product of distillation of the mash of fermented grain, usually of a mixture of corn, wheat, and rye, and at least four years old. Whisky contains from 47 to 53 per cent of alcohol by volume. It should be four years old, because some of the side-products (fusel oil, for example) are deleterious, but on aging four years this fusel oil will have combined with the other constituents of whisky to produce an aromatic substance which in itself is practically harmless.

SPIRITUS VINI VITIS—Brandy

(Sp. Vin. Vit.)

An alcoholic liquid obtained by the distillation of the fermented juice of sound ripe grapes and containing, at 15.56° C., not less than 48 per cent and not more than 54 per cent, by volume, of C_2H_5OH.

It must have been stored in wood containers for a period of not less than four years.

Summarized Description.

Amber-colored liquid; characteristic odor and taste; sp. gr. 0.933 to 0.921. For details, see U.S.P., p. 359.

For *tests for identity* and for *impurities* (same as Whisky), see U.S.P., p. 359.

Remarks.—The old pharmacopœial name for brandy was *spiritus vini gallici*, meaning "spirit of French wine." As some of the medicinal brandy used in this country is made in California, the present Latin name *spiritus vini vitis* or "spirit of grape wine" avoids misrepresentation.

The elaborate chemical tests provided for whisky and brandy by U.S.P. XI are designed to distinguish the genuine distilled and properly aged product for medicinal use from the inferior "blended" whiskies and brandies.

Ethyl Oxide $(C_2H_5)_2O$.—This product is official as in two grades.

ÆTHYLIS OXIDUM—Ethyl Oxide

(**Æthyl. Oxid.**—Solvent Ether)

$C_4H_{10}O$. $C_2H_5.O.C_2H_5$. Molecular weight, 74.08

Ethyl Oxide contains from 96 to 98 per cent of $(C_2H_5)_2O$, the remainder consisting of alcohol and water.

Caution.—Solvent ether must not be used for anesthesia. Only Æther (see below) may be used for anesthetic purposes.

Storage.—Preserve in partly filled, well-closed, light-proof containers, in a cool place, remote from fire.

Summarized Description.

See Æther.

For *tests for identity* and for *impurities*, see Æther.

ÆTHER—Ether

$C_4H_{10}O$. $C_2H_5.O.C_2H_5$. Molecular weight, 74.08

Ether contains from 96 to 98 per cent of $(C_2H_5)_2O$, the remainder consisting of alcohol and water.

Caution.—Ether to be used for anesthesia must be preserved only in small, well-closed containers, and is not to be used for this purpose if the original container has been opened longer than twenty-four hours.

Storage.—Preserve in partially filled, well-closed, light-proof containers, in a cool place, remote from fire.

Summarized Description.

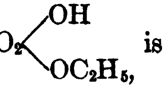
Transparent, colorless, mobile liquid; characteristic odor; burning, sweetish taste; volatile and inflammable; vapor explosive; slowly oxidized by action of air, etc. with formation of peroxides; soluble in about 12 volumes of water; miscible with alcohol, benzene and chloroform; specific gravity, 0.713 to 0.716 at 25° C.; boiling point 35° C. For details, see U.S.P., p. 37.

For *tests for identity* and for *impurities* (acid, peroxides, aldehydes and ketones), see U.S.P., p. 37.

Remarks.—Two forms of ether are included in U.S.P. XI, Æther and Æthylis Oxidum. The former is what is ordinarily called *ether for anesthesia*, while the latter is known as *solvent ether*. Comparison of the two monographs in U.S.P. XI will indicate the care taken to provide for the absolute purity of anesthetic ether. Ethyl oxide is designed only for solvent purposes and it must not be used as an anesthetic. While ether was known to Raymond Lully (1253–1315), the present method of manufacture was devised by Valcrius Cordus in the middle of the fifteenth century. It is made by treating alcohol with sulfuric acid and distilling immediately.

As explained on p. 636, the reaction may be simply expressed as being produced by taking water away from alcohol, sulfuric acid acting as the dehydrating agent. This theory of ether formation proposed by Fourcroy and Vauquelin (1797) was accepted until later investigations proved that while true as to ultimate results, the actual process was not so simple as the mere removal of water by mechanical means. The factor contributing to the rejection of the theory was the fact that if the water was absorbed by the sulfuric acid, it would be closely retained by same, when, as a matter of fact, it is noted that a portion of the water distils over with the ether.

The next theory was the "contact theory" of Mitscherlich, that the ether production was due to catalysis, the latter word a term found very convenient by chemists for the first half of the last century for explaining chemical changes which were not really understood. (See p. 407.)

The discovery of the real process was made by Liebig (1839), who proved that, during the formation of ether, an intermediate product, ethyl-sulfuric acid,  $SO_2 \begin{cases} OH \\ OC_2H_5 \end{cases}$, is produced.

This is sometimes called *"sulfovinic acid,"* and forms salts, one of which, sodium sulfovinate, enjoyed medical prominence some years since.

Liebig's discovery of ethyl-sulfuric acid was supplemented by the researches of Williamson (1850), whose complete theory of ether formation is now accepted as truth.

According to this, alcohol treated with sulfuric acid forms ethyl-sulfuric acid and water (equation *a*). This ethyl-sulfuric acid comes in contact with more alcohol, liberating ether and sulfuric acid (equation *b*):

$$\begin{aligned} &(a)\ C_2H_5OH + H_2SO_4 = C_2H_5SO_4H + H_2O. \\ &(b)\ C_2H_5SO_4H + C_2H_5OH = (C_2H_5)_2O + H_2SO_4. \end{aligned}$$

It will be noted that the above reaction finishes with as much acid as it began with, and this is a fact, a small quantity of sulfuric acid being capable of etherizing a large quantity of alcohol.

The only reason why the same sulfuric acid cannot be used indefinitely is the fact that the acid finally becomes so greatly diluted with water that it is incapable of further chemical action.

As to the practical details of ether formation, the sulfuric acid is placed in a suitable container (still body), gently warmed, and upon it the alcohol is allowed to trickle slowly. Contact of the alcohol with the acid is followed by the formation of ether, which is immediately distilled. The distillate usually contains about 74 per cent of ethyl oxide, and in this form was official in the Pharmacopœia of 1880. The greater portion of the alcohol can be removed by cautious distillation, and ether, U.S.P., which was called *æther fortior* in U.S.P. 1880, is directed to contain from 96 to 98 per cent of ethyl oxide.

Ether can be made from Pintsch gas, a product of the destructive distillation of petroleum. With the use of tax-free alcohol, however, ether can be made cheaper from that source than from Pintsch gas. It may also be prepared by passing the vapor of alcohol over aluminum oxide or alum heated to a suitable temperature (200°–250° C.).

Ether is a clear, limpid liquid of specific gravity 0.716, boiling at 35° C., and as it is exceedingly volatile, must be kept in tightly-closed bottles away from a flame. It is used in pharmacy as a solvent, being the menstruum formerly directed in the preparation of the oleoresins.

Some samples of ether have been known to explode as the last portions are being distilled. This phenomenon is due to presence of peroxides in the sample distilled and it will be noted above that the present Pharmacopœia gives a test for peroxides. The presence of peroxides in ether has produced harmful effects when the contaminated ether was used as an anesthetic and it is imperative that Ether U.S.P. be protected from this deterioration which is apparently due to the oxidizing influence of atmospheric oxygen. The best remedy for this deterioration seems to be the copper coating of the interior surface of the tin container. On the other hand, Gold and Gold state after extensive anesthesia experiments that Ether U.S.P. X stored in large drums for as long a time as sixty-eight days after the first opening shows no deterioration products and exhibits no difference in anesthetic action from that stored in small cans.

Its medicinal use is as an anesthetic, while in proper doses it acts as a sedative. Gwathmey has been very successful in producing anesthesia by rectal injections of ether dissolved in vegetable oils.

Dose.—1 cc. (15 minims).

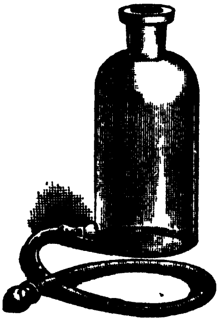


Fig. 266.—Nasal douche bottle.

Syrup of ether of the former editions of the French Codex is well adapted for administration of ether as a sedative. This is made by agitating 500 parts of syrup with 30 parts of ether in a bottle provided with an orifice at the bottom (the Thudicum nasal douche bottle, Fig. 266, with rubber tube replaced by a cork). Ether is macerated with the syrup for five or six days with occasional agitation; then it is allowed to stand, and the clear syrup drained off from the ethereal mixture, which floats on the surface. This, the only satisfactory way of making syrup of ether, has been replaced by a simpler recipe in the last edition of the Codex.

Two much used preparations of ether are *Spirit of Ether*, N.F. (p. 205) and *Compound Spirit of Ether*, N.F. (p. 205).

The following esters of ethyl hydroxide are important pharmaceuticals.

SPIRITUS ÆTHYLIS NITRITIS—Spirit of Ethyl Nitrite

(Sp. Æth. Nitrit.—Spirit of Nitrous Ether, Sweet Spirit of Nitre)

Spirit of Ethyl Nitrite is an alcoholic solution of ethyl nitrite containing not less than 3.5 per cent and not more than 4.5 per cent of C_2H_5ONO.

Storage.—Preserve in small, well-filled and tightly-stoppered bottles, in a cool, dark place, remote from fire.

Condensed Recipe (U.S.P. IX).

Mix 40 cc. of sulfuric acid with 120 cc. of water and after cooling, add 170 cc. of diluted alcohol and chill in a freezing mixture. Add to this liquid little by little a solution of 100 Gm. sodium nitrite, in 280 cc. of water. Separate the ethyl nitrite resulting from the reaction and wash with iced water, then with a chilled sodium carbonate solution and lastly dry with cold dehydrated potassium carbonate. The ethyl nitrite thus purified is poured into 500 Gm. alcohol contained in a tared flask and the solution is then weighed. Having thus ascertained the weight of the ethyl nitrite, add enough alcohol to make the finished spirit weigh twenty-two times as much as the ethyl nitrite used.

Summarized Description.

Clear, mobile, volatile inflammable liquid; pale yellow or faint green-yellow color; fragrant ethereal odor; sharp burning taste; neutral to litmus when fresh; becomes acid on exposure to light and air; sp. gr. 0.823; boils under proper conditions at 65° C. For details, see U.S.P., p. 350.

For *tests for identity* and for *impurities* (free acid, aldehyde), see U.S.P., p. 350.

Assay.—A volumetric *nitrite* assay replaces the gasometric assay of U.S.P. X. For details, see U.S.P., p. 350.

Remarks.—The manufacture of this spirit, as already outlined on p. 637, is performed by treating alcohol with nitrous acid in the presence of sulfuric acid. Nitrous acid itself is an unstable compound, hence in the official preparation it is obtained by treating sodium nitrite with sulfuric acid. Besides, in this and all other esters, a catalytic agent (usually sulfuric acid) is necessary.

The present Pharmacopœia gives no recipe for the manufacture of this important pharmaceutical. The recipe of U.S.P. IX provided that the reaction take place in a vessel surrounded by a freezing mixture, and that the ethyl nitrite formed (insoluble in and lighter than water) be separated from the aqueous layer, freed from acid by treatment with sodium carbonate solution, and from water by use of exsiccated potassium carbonate, and then mixed with twenty-one times its weight of alcohol.

In the process of 1890 the reaction takes place at normal temperatures, and the ethyl nitrite is separated by distillation, the details being as follows:

In a capacious flask is placed sodium nitrite dissolved in water and the alcohol. The flask is tightly fitted with a two-hole cork, through one hole of which passes a separatory funnel, while through the other passes a glass tube connected with an appropriate series of condensers. The sulfuric acid is diluted with water, and while still warm the mixture is allowed to trickle on the sodium nitrite solution in the flask through the separatory funnel.

This causes the following reactions:

$$2NaNO_2 + H_2SO_4 = Na_2SO_4 + 2HNO_2.$$
$$C_2H_5OH + HNO_2 = C_2H_5NO_2 + H_2O.$$

The ethyl nitrite liberated, being very volatile, passes over into the condenser, from which it emerges as a light yellow liquid, having the odor of apples, boiling at 18° C., and with specific gravity 0.900 at 15° C. From this ethyl nitrite traces of acid are removed by washing with a cold solution of sodium carbonate, and the ester is then freed from water by treating with dried potassium carbonate and finally mixed with twenty-one times its own weight of alcohol.

In order to obtain a good yield of the exceedingly volatile ethyl nitrite great care must be taken for thorough condensation. This is best accomplished by the apparatus shown in Fig. 267, where the vapors are first passed up a tall tube and then passed down in the smaller flask, in transit passing through a layer of ice and salt. By such a method a yield as large as 52 Gm. has been obtained from 55 cc. alcohol, the theoretic yield being 67 Gm. of nitrite from 55 cc. alcohol.

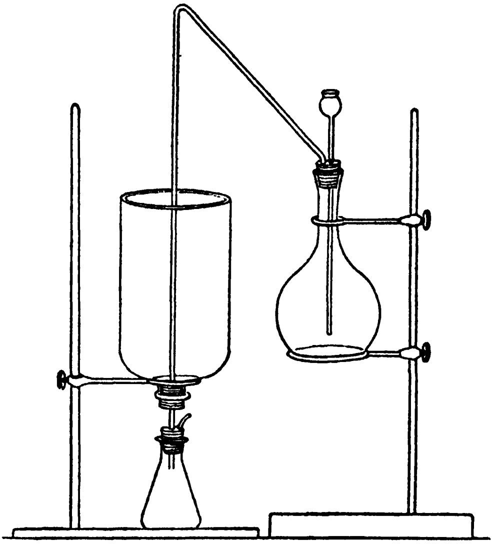


Fig. 267.—Upright condenser for spirit of nitrous ether, U.S.P. 1890.

The actual operation runs smoothly, provided due care is taken that the ethyl nitrite passes over regularly and without sudden rushes. This is accomplished by constantly agitating the reaction flask. If this is not done, the liquid in the flask forms two layers, the sulfuric acid being below and the sodium nitrite solution above. If these two layers are permitted to form, agitation may result in a sudden production of large quantities of ethyl nitrite with sufficient force to cause an explosion. The temperature of the reaction is usually sufficient to distil over all the ethyl nitrite formed. However, it is a matter of wisdom to finish the operation after the reaction appears to have ceased, by gently warming the mixture by means of a water bath.

The finished spirit of nitrous ether is an alcoholic solution of pure ethyl nitrite, and does not represent the original *sweet spirit of nitre*, which was prepared by distilling alcohol with a mixture of nitric and sulfuric acids. The alcohol in the latter case acts as a reducing agent on the nitric acid, and, inversely, the nitric acid oxidizes certain portions of alcohol, with formation of aldehyde. The reactions are as follows:

$$CH_3CH_2OH + HNO_3 = CH_3CHO + HNO_2 + H_2O.$$
$$C_2H_5OH + HNO_2 = C_2H_5NO_2 + H_2O.$$

Fresh spirit of nitrous ether contains 4 to 5 per cent of ethyl nitrite, and as it rapidly deteriorates on standing, should be either freshly prepared or assayed from time to time.

Ethyl Nitrite, $C_2H_5NO_2$, is now available in sealed ampuls, for use in making fresh sweet spirit of nitre.

Sweet spirit of nitre, as the preparation is popularly called, is valuable as a febrifuge and diuretic.

Dose.—2 cc. (30 minims).

Æthylis Acetas (N.F. VI), or *Acetic Ether,* contains at least 96 per cent by volume of ethyl acetate, $C_2H_5C_2H_3O_2$. The method of manufacture is similar to that of ethyl nitrite, namely, treating alcohol with sodium acetate and sulfuric acid by the following reaction:

$$C_2H_5OH + NaC_2H_3O_2 + H_2SO_4 = C_2H_5C_2H_3O_2 + NaHSO_4 + H_2O.$$

The sodium acetate and alcohol are mixed in the distilling flask and the sulfuric acid allowed to trickle in from a separatory funnel, the mixture warmed, and the resulting ethyl acetate distilled. Whitaker reports the successful production of acetic ether by distilling a mixture of alcohol and acetic acid (15 per cent and under), using a very dilute sulfuric acid as catalyst.

Acetic ether is a liquid of very delightful odor, and is one of the most popular of the fruit ethers used in preparing artificial flavoring extracts, the other ethers utilized for the purpose being butyric ether, amyl acetate, and pelargonic ether. (See p. 257.)

Acetic ether is of considerable value in organic chemistry as a crystallizing solvent. It has but little medicinal use but is sometimes given as a stimulant in 15-minim doses.

Ethyl Sulfate $(C_2H_5)_2SO_4$.—This is a constituent of the ethereal oil.

Oleum Æthereum (N.F. VI), or *Ethereal Oil,* is manufactured by treatment of alcohol with sulfuric acid, allowing the mixture to macerate for twenty-four hours, then pouring same into a retort, and distilling the mixture until the frothy residue of the retort rises to the point where there is danger of it running over. This reaction yields varying quantities of ethyl sulfate and ethyl sulfovinate, and the resulting product, called "*heavy oil of wine,*" is dissolved in an equal volume of ether.

In the process large quantities of ether are formed, for it will be noticed that the product is manufactured by a method very similar to that of the manufacture of ether and with exactly the same constituents, the difference in the manufacture being summed up briefly as follows: alcohol plus sulfuric acid plus immediate distillation gives ether. Alcohol plus sulfuric acid plus distillation, after standing, gives ethereal oil.

The yield of ethereal oil is about 20 cc. of the Formulary product from 1100 cc. alcohol, an output so small as to be scarcely worth the pharmacist's time to manufacture. The very fact, however, that the yield is small makes the ethereal oil very expensive, and hence liable to adulteration, and it is said that the larger amount of the so-called "ethereal oil" on the market consists merely of the last distillate in the process of the manufacture of ether, and even this is sometimes adulterated, one of the usual adulterants being castor oil, which liquid has about the same specific gravity as ethereal oil. This falsification, however, can be easily detected by reason of the permanent greasy stain that such ethereal oil will leave on filter paper, whereas true ethereal oil is uniformly volatile. Ethereal oil is a light yellow liquid, having a peculiar penetrating odor, used as a constituent of *compound spirit of ether,* N.F., and is in itself a stimulant.

The manufacture of ethereal oil gives interesting proof of the presence of carbon in alcohol, the residue from the distillation of a mixture of pure sulfuric acid and alcohol consisting primarily of carbon.

Æthylis Aminobenzoas (U.S.P.) or *Benzocaine* can best be considered among the benzoic acid derivatives (p. 797).

Æthylis Chaulmoogras (U.S.P.) will be discussed in connection with chaulmoogra oil (p. 736).

Acetaldehyde is the aldehyde of ethyl alcohol, and its original name has been shortened and employed as the name for the entire class of aldehydes, even as the class called alcohols are named after the original type, grain alcohol.

Aldehyde was discovered by Fourcroy and Vauquelin in 1800. Liebig, observing that aldehyde differed from alcohol in the loss of hydrogen atom, named the finished product "alcohol dehydrogenatus." By combining the first syllables of the two words the name aldehyde was devised.

It will be noticed that the aldehydes are not named after the hydrocarbons from which derived, but from the acids they yield on oxidation. Thus the aldehyde under consideration is never called ethyl aldehyde, but acetaldehyde, likewise the aldehyde of methyl is not called methyl aldehyde, but formaldehyde, because eventually yielding formic acid.

Ordinary aldehyde is CH_3CHO; like other aldehydes, it is made by the oxidation of the corresponding alcohol—in this case, ethyl alcohol. Ethyl alcohol is C_2H_5OH, and its formula can be written CH_3CH_2OH, or even CH_3CHHOH.

Suppose this be oxidized by bringing it in contact with some substance yielding oxygen, like potassium or sodium dichromate and sulfuric acid—we get a reaction like the following, the underscored hydrogen and oxygen atoms separating as water, the new oxygen atom going into the compound:

$$CH_3CH\underline{HOH} + O = H_2O + CH_3CHO \text{ (acetaldehyde).}$$

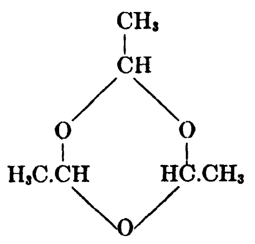
The manufacture of aldehyde is accomplished by treating ethyl alcohol with a mixture of potassium dichromate and sulfuric acid, a very simple and pretty experiment. The orange-red solution of chromic acid formed when potassium dichromate and sulfuric acid are mixed shows the process of oxidation by changing to green as it parts with its oxygen, the green color being due to the formation of chromium sulfate, $Cr_2(SO_4)_3$. Aldehyde is a liquid of characteristic odor, boiling at 21° C.

It is not official, but its polymer, paraldehyde, is accorded pharmacopœial recognition.

PARALDEHYDUM—Paraldehyde

(**Paraldehyd.**—Paracetaldehyde)

$C_6H_{12}O_3$



Molecular weight, 132.09

A polymer $[(CH_3.CHO)_3]$ of acetaldehyde.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless transparent liquid; strong, characteristic but not unpleasant odor; disagreeable, burning then cooling taste; soluble in 8 volumes of water; miscible with alcohol, chloroform, and ether; sp. gr. 0.990; boils at 120° to 125° C., congeals not lower than 11° C. For details, see U.S.P., p. 277.

For *tests for identity* and for *impurities* (fusel oil derivatives, amyl alcohol, sulfate, chloride, free acid and acetaldehyde), see U.S.P., p. 278.

Remarks.—This body represents the condensation of 3 molecules of aldehyde, hence has the formula $(C_2H_4O)_3$.

This is the first example of condensation we have considered, and it is of interest to know that such does not merely mean the compression of 3 molecules of a substance into 1 molecule of a new compound, but that in this process of changing, the character of the compound becomes considerably altered. Thus to paraldehyde is given the structural formula shown above.

The condensation of aldehyde to paraldehyde is accomplished by treating the former with hydrogen chloride or with phosphoric acid. Paraldehyde is a liquid of peculiar, pungent odor, specific gravity of 0.99, boiling between 120° and 125° C. It is a sedative and hypnotic of particular value in cases of delirium tremens.

Dose.—2 cc. (30 minims).

CHLORALIS HYDRAS—Chloral Hydrate

(**Chloral. Hydr.**—Chloralum Hydratum, Chloral)

$C_2H_3O_2Cl_3$. $CCl_3CH(OH)_2$. Molecular weight, 165.39

Chloral Hydrate contains not less than 99.5 per cent of $C_2H_3O_2Cl_3$.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Rhombohedral, colorless crystals; aromatic, penetrating, slightly acrid odor; bitterish caustic taste; slowly volatile; soluble in about 0.25 part of water, in about 1 part of alcohol, in about 3 parts of chloroform, and in about 1.1 parts of ether; also soluble in fixed oils and in oil of turpentine; decomposed by alkalis into chloroform and a formate. For details, see U.S.P., p. 117.

For *tests for identity,* and for *impurities* (chloral alcoholate, chloride, carbonizable substances) and for *assay,* see U.S.P., p. 117.

Remarks.—Chloral hydrate was discovered by Liebig in 1832, but was considered merely as an interesting chemical rarity until its real value as a sedative was discovered in 1869 by Liebreich.

The former pharmacopœial name, *chloral,* is a misnomer, as the true chloral is a liquid which, on addition of 1 molecule of water, forms the crystalline official substance.

Chloral is an aldehyde, the three hydrogen atoms of whose methyl group are replaced by chlorine, as shown by comparison of formulas:

$$\underset{\text{Aldehyde.}}{CH_3CHO} \qquad \underset{\text{Chloral.}}{CCl_3CHO}$$

Chloral is made by passing chlorine gas through alcohol. Chlorine acts as an oxidizing agent—that is, it is one of those substances by which oxygen can be brought in contact with and united to a body. We have seen just above that alcohol, when oxidized, is converted into aldehyde. When chlorine is employed as the oxidizing agent, it also replaces the hydrogen of the aldehyde forming chloral. The stages of the process are:

$$\underset{\text{Alcohol.}}{CH_3CHHOH} \rightarrow \underset{\text{Aldehyde.}}{CH_3CHO} \rightarrow \underset{\text{Chloral.}}{CCl_3CHO}$$

The complete equation of the manufacture of chloral from alcohol is as follows:

$$\begin{aligned} CH_3CH_2OH &+ Cl_2 = CH_3CHO + 2HCl.\\ CH_3CHO &+ Cl_6 = CCl_3CHO + 3HCl.\end{aligned}$$

In manufacturing chloral by this process there is usually produced, besides chloral hydrate, a body, chloral alcoholate, $CCl_3CH\begin{matrix}-OH\\-OC_2H_5\end{matrix}$, the therapeutic effect of which is quite harmful, and hence great caution should be taken to avoid same in official chloral. A test for its detection is given in U.S.P. XI.

Chloral alcoholate is removed during the manufacture of chloral hydrate by upright distillation from concentrated sulfuric acid. This decomposes the alcoholate, while pure chloral is unchanged.

Chloral hydrate is a white solid, occurring in crystals or in white amorphous scales. It is very soluble in water.

As stated above, chloral hydrate is quite soluble in water, and, therefore, it is used to prepare a so-called "100 per cent solution," that is, a solution of 1 avoirdupois ounce to a fluidounce. However, it is scarcely worth while to keep the solution on hand, as it can be so easily prepared, and, moreover, the solution spoils on standing, the chloral decomposing into formic and hydrochloric acids.

Chloral hydrate should never be dispensed in alkaline solution, as during the reaction chloroform is produced:

$$\underset{\text{Chloral.}}{CCl_3CHO} + \underset{\substack{\text{Potassium.}\\\text{hydroxide.}}}{KOH} = \underset{\text{Chloroform.}}{CHCl_3} + \underset{\substack{\text{Potassium}\\\text{formate.}}}{KCOOH}$$

This is a method of making very pure chloroform.

Chloral hydrate is one of the most valuable hypnotics, but, on the other hand, its abuse is one of the most dangerous of the many drug habits.

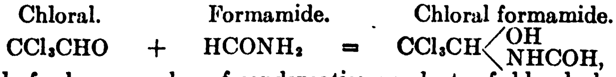
Dose.—600 mg. (10 grains).

Chloral hydrate, when rubbed with camphor, thymol, or menthol, is converted into a thick, viscid liquid, the former, under the name *chloral camphor*, has considerable vogue as a local sedative for gumboils and the like, and, according to the National Formulary, is made by warming together equal quantities of chloral and camphor until liquefied.

To these phenomena, due to the production of a combination having a melting point less than any of its ingredients is given the subject title of *eutectics*. Fusible metals described on page 596, are also considered as illustrations of eutectics.

Quite a number of derivatives of chloral are used as medicines.

Chloral Formamidum (U.S.P. VIII), or *Chloral Formamide*, is made by treating anhydrous chloral with formamide, as expressed in the following equation:



$$\underset{\text{Chloral.}}{CCl_3CHO} + \underset{\text{Formamide.}}{HCONH_2} = \underset{\text{Chloral formamide.}}{CCl_3CH\begin{matrix}/OH\\ \backslash NHCOH\end{matrix}},$$

and is typical of a large number of condensation products of chloral where the group $-C\begin{matrix}-H\\=O\end{matrix}$ is converted into the group $-C\begin{matrix}-H\\-OH\\-R,\end{matrix}$ "R" meaning any radical with one free bond.

Chloralformamide (or *chloralamide*, as it is sometimes called) is used as a hypnotic, in 15-grain doses.

Ural, or *Chloralurethane*, $CCl_3\begin{matrix}/OH\\ \backslash NH-COOC_2H_5,\end{matrix}$ is made by the combination of chloral and urethane and precipitation of the crystals from the reacting liquid by addition of concentrated hydrochloric acid.

Ural is in the form of transparent crystals melting at 103° C., insoluble in water, and used as a hypnotic. *Somnal* is ethylated ural. (See page 756.)

Hypnal is a mixture of *chloral* (45 per cent) and *antipyrine* (55 per cent). It melts at 58° C., and is used as a hypnotic in 15-grain doses.

Acetic Acid (CH_3COOH).—This important compound was known to the ancients in the form of vinegar, a product of the fermentation of wine. The concentrated form of acetic acid was not known until 1700, when prepared by Stahl, its production being accomplished only after it was discovered that one of the products of the destructive distillation of wood was acetic acid, this discovery being made by Glauber in 1648, who called the finished product *wood vinegar.*

The chemical analysis of absolute acetic acid was not accomplished until 1814, when Berzelius gave careful study to the structural character of the compound.

Acetic acid occurs naturally in the sap of some plants, is usually a constituent of sweat, and is found as organic esters in some oils; thus, croton oil contains acetin (glyceryl acetate).

Acetic acid has been produced by synthesis from carbon disulfide.

Carbon disulfide plus chloroform gives carbon tetrachloride, CCl_4.

This body, under treatment with metallic sodium, gives ethylene chloride, $C_2H_4Cl_2$, and eventually ethane hexachloride, C_2Cl_6. Ethane hexachloride treated with water yields trichloracetic acid, CCl_3COOH, and this, by reduction, gives acetic acid.

Acetic acid is now made synthetically in commercial quantities from acetylene, and from ethylene.

Most acetic acid, however, is made by the distillation of wood or by the oxidation of alcohol.

The latter, when diluted and under the influence of the mother of vinegar, *Mycoderma aceti,* is converted into vinegar, which represents a weak acetic acid. The commercial acetic acid, however, is produced by the destructive distillation of wood.

As already explained on p. 649, wood, on being subjected to heat, yields a tarry distillate, called crude pyroligneous acid (*pyros,* meaning fire, and *lignum,* wood), which is composed chiefly of wood alcohol, acetic acid, and acetone.

The separation of acetic acid from this distillate has already been given, so suffice it to say that a very large quantity of acid is produced by such treatment of wood, and it has been found that the great heat formerly thought necessary to decompose same is unnecessary.

Acetic acid can best be prepared by cutting oak wood in appropriate-sized billets, putting into a retort, and heating under 218° C.; at this temperature wood does not char and, except for darkening in color after the process, appears as original wood. The residue is simply dried, and is then sold for fuel.

Acetic acid is official in three distinct strengths.

ACIDUM ACETICUM GLACIALE—Glacial Acetic Acid

(Acid. Acet. Glac.)

Glacial Acetic Acid contains not less than 99 per cent of $HC_2H_3O_2$.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

Clear colorless liquid; strong odor like vinegar; pungent acid taste; miscible with water, alcohol, or glycerin; sp. gr. 1.047 to 1.050; boils at 117° to 118° C.; congeals at about 14.5° C. For details, see U.S.P., p. 14.

Tests for identity and for *impurities* like those for acetic acid. For *assay* see U.S.P., p. 14.

Remarks.—This glacial acetic acid must contain at least 99 per cent CH_3COOH, and is called "glacial," because at temperatures below 15° C. it becomes solid, like ice. Some manufacturers have put upon the market an acetic acid labeled "glacial," but on careful examination of the label it is found that in smaller type are the words 80 per cent. That such procedure is dishonest goes without saying. Glacial acetic acid is very valuable as a solvent for a great diversity of substances; thus it dissolves resins, glue, and a large number of other organic bodies. Its use in this way, however, must be with caution, as there is strong likelihood of its forming chemical combinations.

ACIDUM ACETICUM—Acetic Acid

(Acid. Acet.)

$C_2H_4O_2$. $CH_3.COOH$. Molecular weight, 60.03

Acetic Acid is an aqueous solution containing **not less** than 36 per cent and not more than 37 per cent of $HC_2H_3O_2$.

Storage.—Preserve in glass-stoppered bottles.

Summarized Description.

Clear colorless liquid; strong odor like vinegar; sharply acid taste; miscible with water, alcohol, or glycerin; sp. gr. about 1.045. For details, see U.S.P., p. 12.

For *tests for identity* and for *impurities* (heavy metals, sulfate, chloride, formic acid, sulfurous acid, empyreumatic substances) and for *assay*, see U.S.P., p. 13.

Remarks.—Acetic acid contains 36 per cent absolute acetic acid, and should be ordered as 36 per cent acid. The ordinary commercial acetic acid, familiarly called "No. 8," is not the pharmacopœial acid. It contains but 29 to 30 per cent of absolute acetic acid. The fact that No. 8 acetic acid is not pharmacopœial was learned by a friend of the writer at considerable expense, inasmuch as he dispensed No. 8 acid when acetic acid was called for, and afterward had to answer the charge of violation of the pure food laws of his State. This should warn all pharmacists to exercise the utmost caution in dispensing commodities under pharmacopœial names, unless they are exactly, the standard prescribed by the Pharmacopœia; it being usually considered in interpretation of such laws that when a pharmacist labels a substance with the pharmacopœial name, he means pharmacopœial strength.

No. 8 acetic acid is so called because one part of same with eight parts of water is supposed to give the strength of ordinary vinegar. *Vinegar* is a 3 to 5 per cent solution of acetic acid, more or less impure, and it is assumed that it is always made by the fermentation of alcoholic liquids. Thus a dilute white wine or cider, when fermented, will yield vinegar. A quick method for making vinegar is Schutzenbach's method; percolating a weak alcohol over oak shavings. Authorities state that by any of these methods no vinegar containing more than 15 per cent acetic acid can be made, and as on the market there are a large number of so-called "cider vinegars," as strong as 20 to 25 per cent, the conclusion is obvious that such are made from commercial acetic acid.

The commercial grading of vinegar is by the awkward denomination of so many "*grains*," and this means the number of grains of alkali necessary exactly to neutralize one ounce of the vinegar.

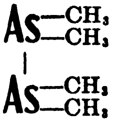
This is even more vague than the average commercial standard, as different authorities say the alkali is sodium carbonate, sodium bicarbonate, potassium carbonate, potassium bicarbonate respectively. Then it is uncertain whether the ounce means troy, avoirdupois, or fluid. If the alkali is potassium bicarbonate, and the "ounce" means fluidounce, "100-grain vinegar" should contain about 12 per cent acetic acid; 50-grain should contain about 6 per cent of acetic acid.

Acetic acid is interesting as a liquid of which the specific gravity is not a criterion of strength. Thus at 15° C. glacial acetic acid has a specific gravity of 1.0562; 85 per cent has a specific gravity of 1.0747; 81 per cent is 1.0755; 80 per cent has a specific gravity of 1.0756, which same specific gravity is possessed by the 79 per cent, 78 per cent, and 77 per cent; 76 per cent has a specific gravity of 1.0755, and from that point on a gradual diminution of specific gravity occurs until 43 per cent has a specific gravity of 1.056—the same specific gravity as the glacial.

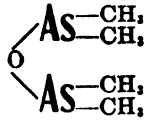
The high specific gravity exhibited by acid containing 77 to 80 per cent CH_3COOH is supposed to be due to the formation, in the solution, of hydroxides of acetic acid.

The *tests* for acetic acid are as follows: when the acid (or an acetate), alcohol, and sulfuric acid are heated together, the mixture gives the pleasant odor of acetic ether. On the other hand, any acetate, when fused with arsenic trioxide on a platinum foil, gives the disgusting odor of cacodyl.

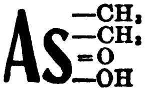
This substance is really a mixture of *cacodyl*, $As_2(CH_3)_4$, and *cacodyl oxide*, $As_2(CH_3)_4O$; the graphic formulas of the two bodies being respectively:



and



These substances, on treatment with mercuric oxide, yield *cacodylic acid* or dimethyl arsenic acid.



ACIDUM ACETICUM DILUTUM—Diluted Acetic Acid

(Acid. Acet. Dil.)

Diluted Acetic Acid is an aqueous solution containing, in each 100 cc., not less than 5.7 Gm. and not more than 6.3 Gm. of $HC_2H_3O_2$.

Storage.—Preserve in glass-stoppered bottles.

Condensed Recipe.

Dilute acetic acid (36 per cent) with enough distilled water to make a 6 per cent product. For details, see U.S.P., p. 13.

Summarized Description.

Miscible with water or alcohol; sp. gr. 1.008; in other respects, like acetic acid. For *assay,* see U.S.P., p. 13.

Remarks.—Diluted acetic acid, contrary to the general rule for diluted acids (that they be 10 per cent), contains 6 per cent absolute acetic acid.

Dose.—2 cc. (30 minims).

SODII CACODYLAS—Sodium Cacodylate

(Sod. Cacodyl.)

$Na(CH_3)_2AsO_2.3H_2O$. Molecular weight, 214.00

Sodium Cacodylate contains not less than 72 per cent and not more than 75 per cent of $Na(CH_3)_2AsO_2$, the remainder consisting chiefly of water.

Storage.—Preserve in air-tight containers.

Summarized Description.

White, odorless, deliquescent prisms or granular powder; soluble in about 0.5 part of water and in about 2 parts of alcohol; melts at 60° C.; anhydrous at 120° C., burns with a bluish flame having garlic-like odor. For details see U.S.P., p. 338.

For *tests for identity*, for *impurities* (monomethyl arsenate, arsenate, phosphate, heavy metals, chloride, sulfate) and for *assay*, see U.S.P., p. 339.

Remarks.—This official substance is made by neutralizing cacodylic acid (prepared as suggested above) with sodium hydroxide. It is a white powder soluble in water, and is used as an alterative and tonic.

Dose.—60 mg. (1 grain).

ACIDUM TRICHLOROACETICUM—Trichloroacetic Acid
(Acid. Trichloroacet.)

$C_2HO_2Cl_3$. $CCl_3.COOH$. Molecular weight, 163.38

Trichloroacetic Acid, dried to constant weight over sulfuric acid, contains not less than 99 per cent of $HC_2Cl_3O_2$.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless, deliquescent, rhombohedral crystals; slight, characteristic odor; very soluble in water, alcohol and ether; not more than 5/100 of 1 per cent of ash. For details, see U.S.P., p. 31.

For *tests for identity*, for *impurities* (chloride and sulfate) and for *assay*, see U.S.P., p. 31.

Remarks.—As chloral represents aldehyde with three hydrogen atoms replaced by three chlorine atoms,

Aldehyde.	Chloral.
CH_3CHO	CCl_3CHO,

so the trichloroacetic acid represents acetic acid with three hydrogen atoms replaced by three chlorine atoms, viz.:

Acetic acid.	Trichloroacetic acid.
CH_3COOH	CCl_3COOH.

Again, as acetic acid can be made by the oxidation of aldehyde (see p. 637), so chloral hydrate on oxidation yield strichloroacetic acid. Trichloroacetic acid is used in dentistry for hardening the gums.

Glycocoll, or amido-acetic acid, and *taurin*, or amido-ethyl-sulfuric acid, must be given passing notice as constituents of oxgall (p. 966). The graphic formulas of these two bodies are:

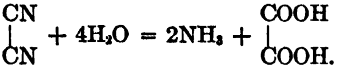
Glycocoll.	Taurin.
CH_2NH_2 | $COOH$	CH_2NH_2 | CH_2SO_3H.

Ethylene Glycol, $CH_2OH—CH_2OH$, is now made upon a large commercial scale by cracking petroleum. It is used as a solvent and as an antifreeze.

The *polybasic acids* are derivatives of the hydrocarbons containing more than one carboxyl group. Thus an acid corresponding to the general formula $R^{II}(COOH)_2$, called dibasic acid, and $R^{III}(COOH)_3$, called tribasic acid, are both illustrations of polybasic acids. The simplest of these is the one which can be considered as derived from ethane.

Oxalic Acid $(COOH)_2$.—This body was long known in the past as the potassium oxalate, which is the constituent of the leaves of several plants, notably *Oxalis perennis*, from which the acid derives its name. It was Scheele, in 1776, who first gave the acid a thorough chemical examination.

Oxalic acid can be made synthetically by several methods. Thus cyanogen, when treated with water, forms ammonia and oxalic acid by the following reaction:



$$\begin{matrix}CN\\ |\\ CN\end{matrix} + 4H_2O = 2NH_3 + \begin{matrix}COOH\\ |\\ COOH.\end{matrix}$$

This is stated because it represents the real method of the synthesis of any acid, the same being formed from hydrocarbons containing one less carbon atom than the acid desired by converting same into chloride, then replacing the chlorine group by the cyanogen group (CN), and then converting the cyanogen group into the carboxyl group by the reaction given above, which is considered as a variety of saponification.

The commercial manufacture of oxalic acid is by the oxidation of either sugar or starch by nitric acid, or by fusing cellulose (sawdust) with potassium hydroxide. The latter is the popular method, the yield being 50 per cent as much as the sawdust employed.

Oxalic acid is not official, although mentioned in the Pharmacopœia as a test solution, both in qualitative testing and in volumetric analysis. It is poisonous, and its antidote is any convenient preparation of lime, thus forming insoluble calcium oxalate.

The potassium binoxalate mentioned above is sold in England as *salt of sorrel* and *salt of lemon*. In the United States, custom has transferred the synonyms to oxalic acid.

BIBLIOGRAPHY

Ethane.—(Structure) Morse, C.A., 22, 1928, 1505.

Ethylene.—(Preparation) Dawson, Jl. Soc. Ch. Ind., 49, 1930, 705B. (Uses) Denny, C.A., 18, 1924, 2542; Regunbal and co-workers, C.A., 22, 1928, 4153; Booth and Campbell, C.A., 23, 1929, 4299.

Ethyl Chloride.—(Manufacture) Groves, Jl. Ch. Soc., 27, 1874, 636; Darling, A., 150, 1869, 216. (Properties) Smith, A.J.P., 4, 1832, 118. (Uses) Ehrmann, Ph. Cent., 33, 1892, 509; Henning, Jl. Soc. Ch. Ind., 39, 1920, 1. (Medical uses.) Baskerville and Hamor, Jl. Ind. Eng. Ch., 5, 1913, 828.

Dichlorethylene.—(Bibliography) Gersdorff, U. S. Dept. Agric., Miscell. Pub., 117, 1932, 1–60. (Uses) Anon., Ph. Era, 63, Dec. 18, 1926, 35; Bauer and Lauth, C.A., 22, 1928, 2221; Fife and Reid, Jl. Ind. Eng. Ch., 22, 1930, 513; Anon., Dr. Circ., 74, Apr., 1930, 50; Mann, C.A., 26, 1932, 4392.

Alcohol.—(Sources) Holland, Ph. Jl., 88, 1912, 569. (History) Babcock, N. R., 9, 1880, 359; Lippmann, Ch. Zt., 36, 1912, 655; 37, 1913, 1313, 1346, 1358, 1419 and 1428; 41, 1917, 865, 883 and 909; 44, 1920, 625; and 46, 1922, 4 and 47, 1923, 757; Pines, A.J.P., 103, 1931, 638; Armstrong, Jl. Soc. Ch. Ind., 52, 1933, 279. (Synthesis) Meldola, Jl. Soc. Ch. Ind., 29, 1910, 737; Pascal, Jl. Soc. Ch. Ind., 45, 1926, 767B; Morgan and Taylor, *ibid.*, 50, 1931, 833B. (Manufacture) Körner, Zt. angew. Ch., 21, 1908, 295; Borde, Ch. Eng., 11, 1910, 167; Adams, Jl. Ind. Eng. Ch., 4, 1912, 8; Anon., C.A., 12, 1918, 1386; von Demuth, Z. angew. Ch., 26, 1914, 786; Rhodes, C.A., 18, 1924, 137; Czadek, C.A., 20, 1926, 2548; Berdeshevsky, C.A., 26, 1932, 2818. (By fermentation) Cagan, C.A., 21, 1927, 149; Veibel, C.A., 26, 1932, 3867; Bernhauer C A., 26, 1932, 1311. (From wood) Kressman, Met. Ch. Eng., 15, 1916, 78; Sadikov, C.A., 20, 1916, 2716; Bedford, Jl. Soc. Ch. Ind., 45, 1926, 580; Leone and Noera, C.A., 22, 1928, 4711; Anon., Jl. Soc. Ch. Ind., 48, 1929, 410. (Properties) Mendelejeff, Pogg. Ann., 138, 1869, 103 and 231; Mariller, C.A., 5, 1911, 2455; Kailan, B., 44, 1911, 2881; Ekecrantz, C.A., 6, 1912, 3093; Finnemore, A.Ph.A., 59, 1911, 77; Swietoslawski and co-workers, C.A., 26, 1932, 3419. (Tests) Lieben, A.J.P., 42, 1870, 176; Vorisek, Jl. Soc. Ch. Ind., 1909, 823. (Alcoholometry) Robertson, Jl. Soc. Ch. Ind., 43, 1924, 806; Bordas and Touplain, C.A., 24, 1930, 3317. (Pharmacology) Hunt, Jl. Ind. Eng. Ch., 17, 1925, 427; Stockard, Lambert and Brooks, C.A., 22, 1928, 4176.

Diluted Alcohol.—(Shrinkage) Mendelejeff, Pogg. Ann., 138, 1869, 103 and 231; Wood, Jl. A.Ph.A., 8, 1919, 730; Foran, Jl. Soc. Ch. Ind., 43, 1924, 338T.

Proof Spirit.—Redwood, Ph. Jl., 4, 1845, 402; Foran, A.J.P., 92, 1920, 11.

Absolute Alcohol.—Noyes, Jl. Am. Ch. Soc., 45, 1923, 857 and Jl. Ind. Eng. Ch., 20, 1928, 119; Winkler, C.A., 10, 1916, 1187; Lyons and Smith, Jl. Soc. Ch. Ind., 45, 1926, 384B; Guinot, *ibid.*, 45, 1926, 459; Cooley, Met. Ch. Eng., 34, 1927, 725; Barbaudy, C. A., 22, 1928, 4711; Smith, Jl. Soc. Ch. Ind., 48, 1929, 449B; von Keussler, Jl. Soc. Ch. Ind., 48, 1929, 261B; Keyes, Jl. Ind. Eng. Ch., 21, 1929, 998; Dietrich, C.A., 24, 1930, 1459; Young, C.A., 25, 1931, 1796; Fritzweiler and Dietrich, Jl. Soc. Ch. Ind., 49, 1930, 344B and Zt. angew. Ch., 45, 1932, 233; Tumentier, C.A., 26, 1932, 1704; Bass, C.A., 26, 1932, 3325.

Denatured Alcohol.—Doran, Jl. Ind. Eng. Ch., 13, 1921, 564 and pamphlet, 48 pages,

Washington, 1932; Whitaker, *ibid.*, 13, 1921, 647; Peffer, C.A., 15, 1921, 2955. (Alcotate) Doran, Dr. Bull., 53, Jan., 1931, 18.

Alcoholic Fermentation.—Pasteur, A.J.P., 32, 1860, 62 and 45, 1873, 119; Buchner, B., 30, 1892, 1110; Hansen, Jl. Soc. Ch. Ind., 8, 1889, 471; Nord, Ch. Met. Eng., 28, 1923, 351; Ling, Jl. Soc. Ch. Ind., 42, 1923, 1234.

Wines.—(History) Ekert, Sch. Wsch. Ch. Ph., 50, 1912, 369 and 385. (Source) Malvezin and Saunier, Comp. rend., 147, 1908, 384; Hewitt, Jl. Soc. Ch. Ind., 47, 1928, 948.

Champagne.—Thudecum, Treatise on Wines, 1896.

Whisky.—(Manufacture) Galleghег, A.Ph.A., 31, 1883, 375.

Ether.—(History) Fourcroy and Vauquelin, A., 23, 1797, 203; Mitscherlich, Pogg. Ann., 21, 273; Liebig, A., 30, 1839, 129; Williamson, Phil. Mag., 38, 1850, 350; Darmstaedter, Jl. prakt. Ch., 120, 1928, 74; Armstrong, Jl. Soc. Ch. Ind., 52, 1933, 279. (Manufacture) Schuberg, A.Ph.A., 55, 1907, 893; Fritzsche, Ch. Ind., 35, 1912, 637; Squibb, Ephemeris, 2, 1884, 590; Wuyts, *ibid.*, 44, 1925, 336B; Bishop, Jl. Soc. Ch. Ind., 43, 1924, 23T; Clark and co-workers, Jl. Am. Ch. Soc., 47, 1925, 2748; Jatkar and Watson, 45, 1926, 168T. (Solubility) Hill, Jl. Am. Ch. Soc., 45, 1923, 1143. (Properties) Kassner, Arch. d. Pharm., 250, 1912, 436; Rosenthaler, C.A., 1, 1907, 2623; Wade and Finnemore, A.Ph.A., 58, 1910, 327. (Explosive) Walton, Am. Dr., 67, 1910, 69; Van Itallie and Van de Zande, Ph. Week, 53, 1916, 1. (Deterioration and preservation) Middleton, Ph. Jl., 113, 1924, 98; Rowe, Jl. Ind. Eng. Ch., 16, 1924, 896; Remy and Neuhart, Jl. Soc. Ch. Ind., 44, 1925, 264B; Nolle, C.A., 22, 1928, 2619; Tikkinen, C.A., 22, 1928, 4721; Nitardy and Tapley, Jl. A.Ph.A., 17, 1928, 966; Van Deripe and co-workers, *ibid.*, 18, 1929, 1228; Palkin and Watkins, Jl. Ind. Eng. Ch., 21, 1929, 863; Hymes and Middleton, Jl. Soc. Ch. Ind., 48, 1929, 869B; Leffmann and Pines, A.J.P., 102, 1930, 58; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1153; Rieche, C.A., 26, 1932, 1124; Gold, Reprint, Anesthesia and Analgesia, Mch.-Apr., 1935. (Pharmacology) van Leeuwen, C.A., 18, 1924, 3217. (Medical uses) Chenisse, C.A., 14, 1920, 3281.

Spirit of Ether.—Wratschko, C.A., 23, 1929, 1212; Schamelhout, C.A., 23, 1929, 4016.

Sulfovinic Acid.—Rabuteau, Am. Dr., 15, 1886, 14.

Anesthetics.—Wood, Jl. A.M.A., 55, 1910, 2229; Baskerville, Am. Dr., 58, 1911, 72 and 108 and C.A., 15, 1921, 1575.

Spirit of Nitrous Ether.—(History) Richtmann and Anderson, Ph. Arch., 2, 1899, 121 and 343; Warington, Ph. Jl., [2], 7, 1865, 7; Redwood, Ph. Jl., [2], 8, 1867, 508. (Manufacture) Dunstan and Dymond, Ph. Jl. [3], 18, 1888, 861; Scoville, Ph. Rev., 17, 1899, 78. (Preservation) Harvey, Ph. Jl., 1, 1841, 354; Roberts, A.J.P., 93, 1921, 320; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1156. (Assay) Curtman, A.Ph.A., 40, 1892, 159; Rae, Ph. Jl., 115, 1926, 633.

Acetic Ether.—(Manufacture) Accarie, Bull. de ph., 1, 1809, 212; Habermann and Brezina, A.Ph.A., 58, 1910, 328; Whitaker, Jl. Soc. Ch. Ind., 42, 1923, 95; Backhaus, C.A., 17, 1923, 2427; Roberts, Jl. Soc. Ch. Ind., 43, 1924, 295T.

Ethereal Oil.—(Manufacture and composition) Hennel, A.J.P., 2, 1831, 73; Squibb, A.Ph.A., 9, 1860, 146 and A.J.P., 29, 1857, 193; Power, Ph. Rund., 9, 1891, 263.

Acetaldehyde.—(Manufacture) Fourcroy and Vauquelin, Ann. de chim., 34, 1800, 318; Liebig, A., 14, 1835, 133; Recoura, Jl. Ch. Soc., 62, 1892, 411; Adams and Williams, Jl. Am. Ch. Soc., 43, 1921, 2420. (Tests) Rogers, A.J.P., 18, 1846, 292.

Paraldehyde.—(Structure) Brühl, A., 203, 1880, 43. (Manufacture) Anon., N.R., 12, 1883, 120; Hatcher and Brodie, C.A., 25, 1931, 4847. (Uses) Cevello, A.Ph.A., 31, 1883, 229.

Chloral.—(History) Lusk, Science, 72, 1933, 271. (Manufacture) Liebig, A.J.P., 4, 1833, 351; Liebreich, Ph. Jl., [2], 11, 1869, 150; Anon., Ch. and Dr., 85, 1914, 336; Durocher, C.A., 20, 1926, 1685. (Alcoholate) Henry, B., 4, 1871, 105 and 435: Anon., A.Ph.A., 22, 1874, 230; Chechik, Jl. A.Ph.A., 19, 1930, 320. (Properties) Guérin, Arch. d. Pharm., 224, 1886, 771. (Incompatibility) Hargreaves, Jl. A.Ph.A., 21, 1932, 571. (Uses) Liebreich, Ph. Jl., [2], 11, 1870, 641.

Chloral Camphor.—Fairthorn, A.J.P., 43, 1871, 447; Browne, Ph. Jl., [3], 4, 1874, 729; Tsakalotus, Jl. de ph. et ch., 12, 1915, 355; Lloyd, Jl. A.Ph.A., 18, 1929, 214.

Eutectics.—Horn, A.J.P., 100, 1928, 558.

Chloral Formamide.—Rabow, Am. Dr., 18, 1889, 190; Harrison, Ph. Jl., [3], 20, 1889, 200; Mering, Am. Dr., 18, 1889, 169.

Ural.—Poppi, Ch. and Dr., 34, 1889, 406; Anon., Am. Dr., 27, 1895, 10.

Somnal.—Radlauer, Ph. Jl., [3], 20, 1889, 341; Lutze, Ph. Zt., 34, 1889, 652.

Hypnal.—Anon., A.Ph.A., 38, 1890, 696.

Acetic Acid.—(History) Babcock, N.R., 10, 1881, 355. (Constitution) Thomlinson, Ch. News, 118, 1919, 23. (Production) Taylor and Lord, A.J.P., 104, 1932, 484. (Synthesis) Pascal, C.A., 21, 1927, 563; Mullin and Hunter, C.A., 26, 1932, 1898; Partridge, Jl. Ind. Eng. Ch., 23, 1931, 482. (Manufacture) Pasteur, A.J.P., 37, 1865, 343; French and Withrow, Jl. Ind. Eng. Ch., 7, 1915, 47; Deschiens, Ch., News, 123, 1921, 155. Armstrong, Jl. Soc. Ch. Ind., 45, 1926, 427T; Conyers, *ibid.*, 49, 1930, 58. ("No. 8" acid) Anon., Dr. Circ., 43, 1899, 153. (Vinegar standard) Rice, Am. Dr., 16, 1887, 138.

Cacodyl and Cacodylates.—Bunsen, A., 46, 1843, 10; Marshall and Green, Am. Ch. Jl., 8, 1886, 128; Martindale, Ph. Jl., 65, 1900, 724; Morgan, Ch. and Dr., 84, 1914, 569; Anon., Dr. Circ., 55, 1911, 255; Ries, Ph. Cent., 61, 1920, 518; Toraude, Ch. and Dr., 95, 1921, 160; Chenisse, Jl. Ph. Ch., 24, 1921, 229.

Trichloracetic Acid.—(Manufacture) Kolbe, Beilstein, 14, 1893, 470. (Uses) Ehrmann, Ch. and Dr., 36, 1890, 557; Davis, C.A., 10, 1916, 496.

Glycocoll.—Benton, Pharm. Era, 10, 1893, 53.

Taurin.—James, Jl. Ch. Soc., 35, 1879, 810.

Ethylene Glycol.—(Manufacture and uses) Taylor and Rinkenbach, Jl. Ind. Eng. Ch., 18, 1926, 676; Armstrong, Jl. Soc. Ch. Ind., 49, 1930, 178. (Toxicity) Hunt, Jl. Ind. Eng. Ch., 24, 1932, 361 and 836; Hanzlik, *ibid.*, 24, 1932, 836.

Oxalic Acid.—(History) Savary (1773) and Scheele (1776), Kopp, 4, 1847, 354. (Synthesis) Berthelot, A., 120, 1861, 254. (Manufacture) Hedenstrom, Ch. Zt., 35, 1911, 853; Mahood and Cable, 11, 1919, 651; Anon., Am. Drug., 69, Jan., 1921, 35; Preen, C.A., 18, 1924, 1564.

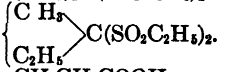
Salt of Sorrel.—Purdie, Ph. Jl., 114, 1925, 132.

CHAPTER XXXVIII

DERIVATIVES OF PROPANE, BUTANE, AND PENTANE

PROPANE

THE propane derivatives of interest are:

Propyl alcohols	C_3H_7OH.
Propyl aldehyde	CH_3CH_2CHO.
Acetone, U.S.P.	$CH_3—CO—CH_3$.
Sulfonmethane, N.F.	$(CH_3)_2C(SO_2C_2H_5)_2$.
Sulfonethylmethane, U.S.P.	 $\left\{\begin{matrix}CH_3\\C_2H_5\end{matrix}\right\}>C(SO_2C_2H_5)_2$.
Propionic acid	CH_3CH_2COOH.
Lactic acid, U.S.P.	$CH_3CHOHCOOH$.
Glycerin, U.S.P.	$C_3H_5(OH)_3$.
Nitroglycerin	$C_3H_5(ONO_2)_3$. (Official in *spirit of glyceryl trinitrate.*)
Glyceryl oleate	Olein and other fats.

Of the above, two propyl alcohols, primary and secondary, are known. The former yields on oxidation propylic aldehyde, while the secondary gives, under the same treatment, the ketone, acetone.

Secondary propyl alcohol (*isopropyl alcohol*) is now obtained in considerable quantities as a by-product of the petroleum and natural gas industries. One commercial form is sold under the name "*petrohol.*" It is used as a denaturant for alcohol and as a solvent for resins and for perfumes. As it is by no means nontoxic its indiscriminate use is unwise.

Propionic aldehyde can be dismissed on the simple statement that it, on oxidation, yields propionic acid, CH_3CH_2COOH.

ACETONUM—Acetone

(Aceton.—Dimethyl Ketone)

C_3H_6O. $CH_3.CO.CH_3$. Molecular weight, 58.05

Acetone contains not less than 99 per cent of $(CH_3)_2CO$.

Storage.—Preserve in well-closed containers, in a cool place, remote from fire.

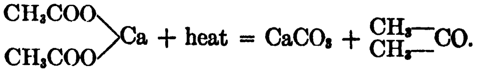
Summarized Description.

Colorless, mobile, volatile liquid; characteristic ethereal odor; pungent sweetish taste; sp. gr. 0.790; miscible with water, alcohol, ether, chloroform and most volatile oils; boils at 56° to 58° C.; inflammable, burning with a nonsooty flame. For details see U.S.P., p. 10.

For *tests for identity*, for *impurities* (empyreumatic substances) and for *assay*, see U.S.P., p. 11.

Remarks.—Acetone is the first representative of the ketones (p. 637) to be studied. It has been long known as one of the products of the destructive distillation of wood. It was not, however, until 1832 that its chemical composition became known through the investigations of Liebig.

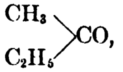
Acetone has been secured from natural sources (the urine and the blood). It can be made by oxidation of secondary propyl alcohol, as already explained on p. 637. Another chemical method of the manufacture of acetone is by the destructive distillation of calcium acetate by the following reaction:



$$\left.\begin{array}{l}CH_3COO\\CH_3COO\end{array}\right\rangle Ca + \text{heat} = CaCO_3 + \begin{array}{l}CH_3-\\CH_3-\end{array}CO.$$

This method is of importance, inasmuch as it is the type of the general manufacture of ketones.

As seen above, calcium acetate yields dimethyl ketone or acetone. If, instead of calcium acetate, a mixture of calcium acetate and calcium propionate be distilled, we get methyl-ethyl ketone,



$$\left.\begin{array}{l}CH_3\\C_2H_5\end{array}\right\rangle CO,$$

while a mixture of calcium acetate and calcium benzoate gives methyl-phenyl ketone. The main commercial source of acetone, however, is the destructive distillation of wood, and the acetone is extracted from the distillate, as has already been explained on p. 649.

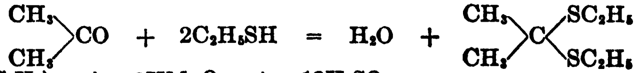
Recently acetone has been obtained upon a commercial scale by the fermentation of carbohydrates with special organisms, such as *Bacillus volutans* and *B. acetoethylicus*. Gokhale reports that the dried Mahua flowers of India yield upon fermentation as much as 5 per cent of acetone. Donath prepares acetone by passing the vapor of ethyl alcohol over heated pyrolusite.

Acetone possesses, in common with all ketones, a number of characteristic reactions; thus it forms crystalline compounds with ammonium bodies, or with potassium bisulfate, and, most striking of all, when treated with hydroxylamine, it forms characteristic bodies called "oximes" (RNOH). It also forms distinct crystalline bodies with phenyl hydrazine, the reagent giving practically similar results with aldehydes. In truth, the two great classes, aldehydes and ketones, are difficult to distinguish from each other, about the only point of difference being that, while aldehydes oxidize to acids, ketones break up into simpler bodies on oxidation.

The reactions above cited are of pharmaceutic interest only inasmuch as hydroxylamine and phenylhydrazine give distinct crystalline bodies with the sugar (these substances being either of aldehyde or ketone character), hence these reagents are used for testing sugars. Legal's reaction based upon the red color produced when acetone is treated with sodium nitroprusside and alkali is used largely in the detection of acetone in urine.

Acetone has but little medical value, its chief use in pharmacy being as a solvent. For this purpose it was formerly used in making the official oleoresins. It yields several products of marked value in medicine, one of which is now official.

Sulfonmethanum (U.S.P. X; N.F. VI), or *Sulfonal*, or diethylsulfon-dimethylmethane, $(CH_3)_2C(SO_2C_2H_5)_2$, is made by treating acetone with ethyl mercaptan and oxidizing the resulting mercaptid with potassium permanganate, the equation being as follows:



$$(CH_3)_2CO + 2C_2H_5SH = H_2O + (CH_3)_2C(SC_2H_5)_2$$

$$5(CH_3)_2C(SC_2H_5)_2 + 8KMnO_4 + 12H_2SO_4 = 5(CH_3)_2C(SO_2C_2H_5)_2 + 4K_2SO_4 + 8MnSO_4 + 12H_2O.$$

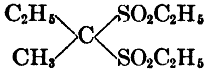
Mercaptan is a liquid of very disagreeable odor, made by treating ethyl bromide with potassium sulfhydrate. It can easily be produced from sulfonal by heating same in a test tube with charcoal, and this affords a simple test for the identification of sulfonal.

Sulfonal is a white, crystalline solid, sparingly soluble in water, and melting at 125° C. It is a valuable hypnotic.

Dose.—750 mg. (12 grains).

SULFONETHYLMETHANUM—Sulfonethylmethane
(Sulfonethylmeth.)

$C_8H_{18}O_4S_2$



Molecular weight, 242.26

Diethylsulfon-methylethylmethane.

Storage.—Preserve in well-closed containers.

Summarized Description.

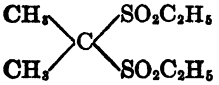
Colorless, lustrous, odorless crystalline scales; bitter in aqueous solution; soluble in about 200 parts of water; also soluble in alcohol or ether; melts between 74° and 76° C.; at higher heat decomposes. For details, see U.S.P., p. 366.

For *tests for identity*, for *impurities* (sulfate, chloride, oxidizable matter), see U.S.P., p. 366.

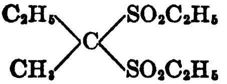
Remarks.—This body, introduced under the name *trional*, differs from sulfonal by having an ethyl group in place of one of the methyl groups of sulfonal, as is shown below. It thus contains three ethyl groups, hence the name, trional. It is made like sulfonal, except that in place of acetone, ethyl-methyl ketone is employed.

Tetronal contains no methyl group, but four ethyls (see compared formulas given below), and it is made like sulfonal, only that diethyl ketone is used in its manufacture instead of acetone (dimethyl ketone). Both trional and tetronal are used as hypnotics in 12-grain doses.

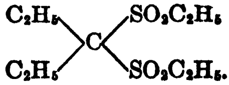
Sulfonal



Trional



Tetronal



Propionic Acid (C_2H_5COOH), discovered by Gottlieb in 1844, can be made by oxidation of primary propionic alcohol, as above stated, by the saponification of ethyl nitrile, CH_3CH_2CN, and by the fermentation of the lactic acid in whey by *Bacterium acidi propionici.* It has no pharmaceutic value, but its derivative, oxypropionic acid, is official under the name of lactic acid.

Three oxypropionic acids are known: ethylidene lactic acid, CH_3—CHOH—COOH; ethylene lactic acid, $CH_2OH—CH_2—COOH$; and sarcolactic acid. The official acid is the one first mentioned.

ACIDUM LACTICUM—Lactic Acid

(Acid. Lact.)

$C_3H_6O_3$. $CH_3.CHOH.COOH$. Molecular weight, 90.05

A mixture of lactic acid and lactic anhydride equivalent to a total of not less than 85 per cent and not more than 90 per cent of $HC_3H_5O_3$.

Storage.—Preserve in well-stoppered bottles.

Summarized Description.

Colorless, hygroscopic, syrupy liquid; acid taste; miscible with water, alcohol or ether; insoluble in chloroform, petroleum benzin or carbon disulfide; sp. gr. 1.206; below 160° C. not vaporized, above 160° C. emits inflammable vapors. For details, see U.S.P., p. 22.

For *tests for identity*, for *impurities* (chloride, sulfate, heavy metals, phosphoric, citric and tartaric acids, sugars, carbonizable impurities, sarcolactic acid) and for *assay*, see U.S.P., p. 23.

Remarks.—This body was discovered by Scheele in 1780 as a constituent of sour milk. Besides in milk, it is found in minute traces in opium, and also is found in gastric juice in that form of dyspepsia we call "sour stomach." It can be made synthetically in several ways.

Milk is a fluid obtained from the cow, and consists of fat (butter), emulsified by means of casein. This emulsion is considerably diluted with water, containing a variety of sugar called sugar of milk or lactose. This sugar of milk, under the influence of certain bacteria found in the air, ferments to lactic acid. The actual method of production from milk is first by removing the butter in churning, then separating the casein by the addition of acid. The liquid remaining after the curd has been removed is called the *whey*, and contains the sugar of milk. If this whey is concentrated and allowed to stand, the milk sugar crystallizes (p. 700), but if the same is allowed to stand until fermentation sets in, lactic acid continues to form until the solution contains 1.6 per cent acid, when the ferment becomes inactive. If the acidity of the mixture is lessened by treatment with zinc carbonate or chalk, the fermentation continues and the addition of carbonate is carried on in actual practice in order to obtain a larger percentage of the acid. Of course, the finished product in such cases is either zinc or calcium lactate, but the acid can be easily freed from the metal by treatment with sulfuric acid.

Lactic acid is now being made commercially by the fermentation of glucose by use of the lactic acid ferment. It is also one of the products obtained in the preparation of alcohol from sawdust (p. 655).

Lactic acid is a thick, syrupy liquid, of specific gravity 1.206. It always contains water, the strength of the official acid being from 85 to 90 per cent. By removing all the water a new body, *lactone*, is formed.

Lactic Acid Ferments.—The micro-organisms producing the lactic fermentation include the bacteria of the Bulgarian bacillus group. There has been quite a vogue for *Bacillus Bulgaricus* in intestinal troubles. The therapeutic value of these ferments is still a subject of controversy.

Syrupus Calcii Lactophosphatis (N.F. VI), is made by mixing 25 Gm. of precipitated calcium carbonate; with 60 cc. lactic acid, previously diluted with 100 cc. water, whereby a solution of calcium lactate is obtained. To this is added 36 cc. phosphoric acid, diluted with 50 cc. water, and the mixture triturated until a perfect solution results. After adding 100 cc. water the liquid is filtered and to the filtrate 50 cc. of orange flower water is added, and 650 Gm. sucrose dissolved therein by cold agitation. Then add enough water to make 1 liter.

It is used as a nutritive tonic in wasting diseases.

Dose.—10 cc. (2½ fluidrachms).

Polyatomic alcohols are those containing more than one hydroxyl group. Thus while alcohol, C_2H_5OH, containing one hydroxyl, is monatomic, glycol, being $C_2H_4(OH)_2$, is diatomic, and glycerin, $C_3H_5(OH)_3$, is triatomic; hence the last two are polyatomic or polyhydric alcohols.

GLYCERINUM—Glycerin

(Glycerin.—Glycerol)

$C_3H_8O_3$. $CH_2OH.CHOH.CH_2OH$. Molecular weight, 92.06

Glycerin is a polyhydric alcohol which contains not less than 95 per cent of $C_3H_5(OH)_3$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Clear, colorless liquid of thick syrupy consistence; slight odor; sweet and then warm taste; miscible with water and alcohol; insoluble in chloroform, ether, benzene, petroleum benzin, carbon disulfide, fixed and volatile oils; sp. gr. about 1.249. For details, see U.S.P., p. 179.

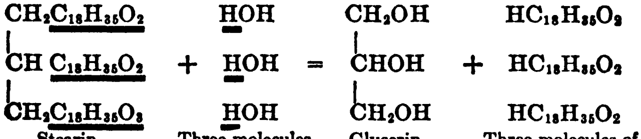
For *tests for identity,* for *impurities* (carbonizable substances, fatty acids, esters, acrolein, glucose, ammonium compounds, sulfate, chloride, oxalic acid, heavy metals and arsenic), see U.S.P., p. 180.

Remarks.—This interesting body was discovered by Scheele in 1779 in the wash water in making lead plaster. It was first analyzed by Pelouze in 1837, while its structural formula was worked out by Wuertz (1855). Its introduction as a commercial commodity was between 1844 and 1850, during which time it was introduced by Price, of England, Sarg, of Vienna, and Robert Shoemaker, of Philadelphia.

Glycerin has been made synthetically and by several methods, none of which is of interest save as establishing the structural formula assigned above. It is obtained commercially from fats, these being derivatives of glycerin with oleic, stearic, and palmitic acids (p. 728).

If a fatty oil, such as olive oil, be treated with lead oxide in the manufacture of lead plaster, a double decomposition occurs, with the formation of lead oleate and the freeing of glyceryl hydroxide, as fully explained on p. 609, and this was the original method of the manufacture of glycerin.

In 1854 Tilgman found that glycerin could be obtained from the fats by treating same with superheated steam, and this is the method generally applied at present, the reaction being:



$$\begin{array}{lclclcl}
CH_2\underline{C_{18}H_{35}O_2} & & \underline{H}OH & & CH_2OH & & HC_{18}H_{35}O_2 \\
| & & & & | & & \\
CH\,\underline{C_{18}H_{35}O_2} & + & \underline{H}OH & = & CHOH & + & HC_{18}H_{35}O_2 \\
| & & & & | & & \\
CH_2\underline{C_{18}H_{35}O_2} & & \underline{H}OH & & CH_2OH & & HC_{18}H_{35}O_2
\end{array}$$

Stearin. Three molecules of water. Glycerin. Three molecules of stearic acid.

This saponification can also be accomplished by treating the fat with diluted sulfuric acid and a catalyst. In the Twitchell process, naphthalene sulfo-oleic acid and similar chemicals are employed and in other processes the catalysts employed are enzymes, notably those from the castor oil bean.

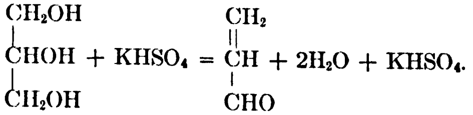
The enormous use of glycerin (as nitroglycerin) during the World War almost exhausted the supply of available fats; hence the production of glycerin by the fermentation of sugar with special micro-organisms (*Saccharomyces ellipsoideus,* for example) was carried on with some success.

Crude glycerin thus obtained has to be purified by distillation in vacuo, although it is said that the chemically pure product can be distilled without decomposition at ordinary atmospheric pressure.

Glycerin is a transparent, viscid liquid, of sweetish taste, of specific gravity about 1.25. As already mentioned, glycerin is a solvent of peculiar value, inasmuch as it is also antiseptic. Goodrich points out, however, that many substances are better antiseptics in aqueous solution than when dissolved in a mixture of glycerin and water. Glycerin is used medicinally as a protective and when used in the form of glycerin suppositories, it acts as a purgative. Glycerin is also much esteemed as an ingredient of domestic cough remedies.

Dose.—4 cc. (1 fluidrachm).

Glycerin, when treated with oxalic acid, yields formic acid and when treated with potassium bisulfate, yields acrolein by the following reaction:

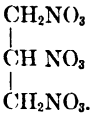


$$\begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + KHSO_4 = \begin{array}{l} CH_2 \\ \| \\ CH \\ | \\ CHO \end{array} + 2H_2O + KHSO_4.$$

Acrolein is the aldehyde of allyl alcohol, has a very disagreeable odor, and is very irritating to the eyes and throat. It is familiar as the disagreeable odor of burning fat.

Nitroglycerin.—This ester of glycerin was discovered by Sobrero in 1847. It is made by placing glycerin in a freezing mixture and allowing a mixture of nitric acid and sulfuric acid to drop down upon it, cautiously stirring the finished product and then diluting.

Like stearin and olein, nitroglycerin is an ester of glycerin. On p. 729 is given the graphic formula of olein and of stearin; to these we will add, for comparison, the graphic formula of nitroglycerin:



$$\begin{array}{l} CH_2NO_3 \\ | \\ CH\ NO_3 \\ | \\ CH_2NO_3. \end{array}$$

Reference to p. 663 will show that the ester, ethyl nitrite, $C_2H_5NO_2$, was made by treating grain alcohol—ethyl hydroxide, C_2H_5OH—with nitrous acid, by the following reaction:

$$C_2H_5OH + HNO_2 = H_2O + C_2H_5NO_2.$$

Even so, the ester, nitroglycerin, $C_3H_5(NO_3)_3$, is made by treating the alcohol, glyceryl hydroxide—glycerin, $C_3H_5(OH)_3$—with nitric acid, HNO_3, by the following reaction:

$$C_3H_5(OH)_3 + 3HNO_3 = 3H_2O + C_3H_5(NO_3)_3,$$

sulfuric acid being used as the dehydrating or catalytic agent (p. 407).

Nitroglycerin in concentrated form is used as an explosive, it being one of the most rapid and dangerous of known explosives (p. 471).

Nitroglycerin, while so dangerous an explosive, possesses an element of safety, inasmuch as it is not easily set off, it being exploded only by being rapidly heated or by concussion, and in order to obtain the best results the latter method is usually employed, the charge of nitroglycerin being placed in contact with a cap of fulminating mercury, which is fired either by a fuse or by electric connection.

The liquid form of nitroglycerin being inconvenient in many cases, explosive modifications of a solid character have been devised. Thus, *dynamite* is a mixture of 1 part of infusorial earth with 3 parts of nitroglycerin.

Nitroglycerin, like all esters, can be saponified by alkali. Thus we have already found that ethyl nitrite, when treated with an alkali, is converted into alcohol and potassium nitrite, so in the same way nitroglycerin treated with sodium hydroxide yields inert glycerin and equally harmless sodium nitrate by the following reaction:

$$C_3H_5(ONO_2)_3 + 3KOH = C_3H_5(OH)_3 + 3KNO_3.$$

This gives a hint as to avoiding explosion if nitroglycerin or its spirit is accidentally spilled.

SPIRITUS GLYCERYLIS TRINITRATIS—Spirit of Glyceryl Trinitrate (Sp. Glyceryl. Trinitrat.—Spirit of Nitroglycerin, Solutio nitroglycerini spirituosa P.I.)

Spirit of Glyceryl Trinitrate is an alcoholic solution containing not less than 1 per cent and not more than 1.1 per cent of $C_3H_5(NO_3)_3$ (molecular weight, 227.06).

Caution.—Great care must be exercised in dispensing, handling, packing, transporting, and storing this spirit, since a dangerous explosion may result if any considerable quantity of it is spilled, and the alcohol wholly or partly lost by evaporation. If, through accident, it is spilled, a solution of potassium or sodium hydroxide must be poured over it at once to effect the decomposition of the glyceryl trinitrate.

Storage.—Preserve in well-closed containers, in a cool place, protected from light and remote from fire.

Summarized Description.

Clear, colorless liquid; alcohol odor; very toxic, hence taste with caution; sp. gr. 0.814 to 0.820. For other tests and for *assay*, see U.S.P., p. 356.

Remarks.—This official is a 1 per cent alcoholic solution of nitroglycerin. It is a colorless liquid, of alcoholic taste. The Pharmacopœia, however, gives warning that utmost care must be exercised when tasting, as even a small quantity is liable to produce violent headache. It is also well to heed the pharmacopœial warning that the spirit must be handled with the utmost caution, for if spilled, the alcohol will evaporate and the explosive properties of the nitroglycerin will be exerted unless an alkaline solution is poured upon it.

Spirit of nitroglycerin is used as a heart stimulant.

Dose.—0.06 cc. (1 minim).

TABELLÆ GLYCERYLIS TRINITRATIS—Tablets of Glyceryl Trinitrate

(Tab. Glyceryl. Trinitrat.—Tablets of Nitroglycerin, Trinitrin Tablets)

Tablets of Glyceryl Trinitrate contain not less than 87.5 per cent and not more than 112.5 per cent of the labeled amount of $C_3H_5(NO_3)_3$, including all tolerances.

Remarks.—This new official tablet is described at length on p. 346.

Dose.—0.6 mg. ($\frac{1}{100}$ grain) of glyceryl trinitrate.

Glyceryl-phosphoric Acid.—In 1845, Gobley discovered in yolk of egg a substance which proved to be a compound of glycerin and phosphoric acid; the structure of which is supposed to be $CH_2OPO(OH)_2$—CHOH—CH_2OH. An isomere of this substance where the phosphoric acid radical is attached to central carbon atom of the glycerin structure is also known. Both of these acids form salts and preparations of these, with calcium glycerophosphate as leading ingredient have become quite popular. At present glycerophosphoric acid is made by the condensation of the two ingredients.

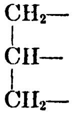
The present National Formulary recognizes *calcium glycerophosphate* (p. 527), *ferric glycerophosphate* (N.F. VI, p. 147), *manganese glycerophosphate* (p. 541), and *sodium glycerophosphate* (p. 495).

Boroglycerin, $C_3H_5BO_3$, is the boric acid ester of glycerin, and is made by heating glycerin with boric acid. For details of operation see Glycerite of Boroglycerin, U.S.P. (p. 181). The official glycerite can be considered as a 50 per cent solution of boroglycerin, as the following calculation shows:

$$\begin{array}{lcccccc} \text{Reaction: } C_3H_5(OH)_3 & + & H_3BO_3 & = & 3H_2O & + & C_3H_5BO_3. \\ \qquad\qquad\quad 92 & & 62 & & 54 & & 100 \end{array}$$

From the molecular weight just given it is seen that 62 Gm. boric acid plus 92 Gm. glycerin give 100 Gm. boroglycerin, and as the pharmacopœial recipe (given on p. 232) directs 310 Gm. boric acid plus 460 Gm. glycerin, that this be heated until 500 Gm. remain, and that this be mixed with 500 Gm. glycerin, it is plain that the above quantities (five times the theoretic amounts) will yield 500 Gm. boroglycerin, and that, therefore, the finished glycerite contains 50 per cent boroglycerin. This is important, inasmuch as boroglycerin is frequently prescribed in 10 per cent, 20 per cent, or 30 per cent solution, and such should be made by properly diluting the official glycerite with glycerin.

Fats are esters of glycerin with oleic, stearic, and palmitic acids. They will be considered in a special chapter as derivatives of the acids just mentioned. As mentioned above, the radical—



$$\begin{array}{l} CH_2— \\ | \\ CH— \\ | \\ CH_2— \end{array}$$

found in glycerin is called *glyceryl*. This is not to be confused with another radical (C_3H_5) having the formula $CH_2{=}CH—CH_2—$, called *allyl*. Allyl is an unsaturated radical, and, therefore, possesses but one free bond, while glyceryl is a saturated radical and has three free bonds. Three compounds of allyl are worth passing notice: *acrolein* (allyl aldehyde), $CH_2{=}CH—CHO$, just described as one of the products obtained on strongly heating glycerin; allyl sulfide, $(CH_2{=}CH—CH_2)_2S$, the odorous constituent of oil of garlic; and, lastly, allyl isothiocyanate (oil of mustard), which will be considered among the cyanogen derivatives (p. 753).

BUTANE

(C_4H_{10})

The butane derivatives of general importance are:

The butyl alcohols	C_4H_9OH.
Chlorobutanol	$Cl_3C—C(CH_3)_2OH$.
Butyl chloral hydrate	$CCl_3CH_2CH_2CHO + H_2O$.
Butyric acids	$CH_3CH_2CH_2COOH$, etc.
Succinic acid	$C_2H_4(COOH)_2$.
Mercury succinimide	$(CH_2CO)_2{:}NHgN{:}(COCH_2)_2$.
Malic acid	$C_2H_3(OH)(COOH)_2$.
Tartaric acid, U.S.P.	$C_2H_2(OH)_2(COOH)_2$.
Erythrol	$CH_2OH(CHOH)_2CH_2OH$.
Erythrol tetranitrate (Erythrol tetranitrate (diluted), U.S.P.)	$CH_2NO_3(CHNO_3)_2CH_2NO_3$.

The haloid derivatives of butane are of no pharmaceutic interest. Butyl alcohols, C_4H_9OH, are found in four forms, for it will be noticed on p. 640 the number of isomeres increase in proportion to the number of carbon atoms in a compound.

Of these butyl alcohols, the primary $CH_3CH_2CH_2CH_2OH$ is of interest as being one of the constituents of crude fusel oil. On oxidation the primary alcohol yields butyric aldehyde, and then the oxidation product of butyric aldehyde, butyric acid. Normal butyl alcohol is now made on a commercial scale by the fermentation of carbohydrates with special organisms.

Tertiary butyl alcohol, $(CH_3)_3COH$, is of interest because its trichlor derivative—$(CH_3)_2CCl_3COH$—is being considerably advertised under the names *chlorctone* or *chlorobutanol.*

CHLOROBUTANOL—Chlorobutanol

(Chlorobut.—Chlorobutol, Acetone-Chloroform)

$C_4H_7OCl_3$. $Cl_3C.C(CH_3)_2.OH$. Molecular weight, 177.43

Trichlor tertiary butyl alcohol, either anhydrous or containing up to about one-half molecule of water.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless crystals; camphoraceous odor and taste; soluble in about 125 parts of water, 0.8 part of 90 per cent alcohol, 8 parts of glycerin, readily soluble in ether, chloroform and in volatile oils.

For *tests for identity* and for *impurity* (chloride), see U.S.P., p. 118.

Remarks.—This is the trichlor derivative of tertiary butyl alcohol. It is made by treating a mixture of chloroform and acetone with caustic alkalis, and is a white crystalline solid, soluble in 125 parts of water, very soluble in alcohol. It is used as a hypnotic and as an antiseptic. It is a constituent of *Odontalgicum,* N.F.

Dose.—0.6 Gm. (10 grains).

Brometone, $(CH_3)_2CBr_3COH$, has been obtained in white crystals melting at 167° C.

Erythrol, $CH_2OH(CHOH)_2CH_2OH$, is obtained from certain algæ and lichens. It can be made synthetically from trioxybutyric acid. Its *tetranitrate* is used as a heart stimulant in place of nitroglycerin and is also employed in certain explosives.

Erythrol Tetranitrate is the chemical, $CH_2NO_3—CHNO_3—CHNO_3—CH_2NO_3$. It is made by treating the tetrahydroic alcohol, erythrol, with a mixture of nitric and sulfuric acids under proper precautions. It is a white powder that is very explosive. It has been introduced into U.S.P. XI in the following diluted form:

ERYTHRITYLIS TETRANITRAS DILUTUS—Diluted Erythrityl Tetranitrate

(Erythrit. Tetranit. Dil.—Diluted Erythrol Tetranitrate, Diluted Tetranitrol)

Diluted Erythrityl Tetranitrate is a mixture of erythrityl tetranitrate and lactose, and occurs as a white powder, or in the form of tablets. The powder contains not less than 47 per cent and not more than 53 per cent of $C_4H_6(NO_3)_4$ (302.08). Tablets of erythrityl tetranitrate do not vary more than 7.5 per cent above and not more than 7.5 per cent below the labeled amount of erythrityl tetranitrate $[C_4H_6(NO_3)_4]$.

Storage.—Preserve in a cool place and protected from light.

Summarized Description.

Erythrol tetranitrate diluted with an equal quantity of lactose. It is partly soluble in alcohol and in ether (the tetranitrate) and in water (lactose). The separated tetranitrate melts at 60° to 61° C. (*Caution*).

For *tests for identity* and for *assay,* see U.S.P., p. 149.

Remarks.—This official is a vasodilator like nitroglycerin. It is introduced in diluted form to facilitate its use in preparing tablets.

Dose.—0.03 Gm. (½ grain).

A derivative of butyric aldehyde ($CH_3CH_2CH_2CHO$) is *butyl chloral hydrate* ($CCl_3CH_2CH_2CHO + H_2O$), which was discovered by Kraemer and Pinner in 1870, who, on its discovery, thought it was the isomeric "*croton chloral hydrate*," and under this name the product was introduced into medicine as a hypnotic. *Dose.*—0.3 to 0.6 Gm. (5 to 10 grains).

Two *butyric acids* are known: (1) $CH_3CH_2CH_2COOH$ (normal).
(2) $(CH_3)_2CHCOOH$ (iso).

The first of these is a constituent of sweat, while its glycerin ester comprises 2 to 3 per cent of butter. From its discovery in butter the name, butyric acid, is obtained.

Butyric ether is the ester of butyric acid made by treating it with ethyl alcohol in the presence of a dehydrating agent. It is a colorless liquid of fruity odor boiling at 121° C., that is used largely in making artificial fruit essences.

Banana oil is a mixture of butyric ether, 1 part; amyl acetate, 1 part, and alcohol 5 parts. It is used largely as a solvent in the gilding industry.

Succinic acid,

$$COOH—CH_2—CH_2—COOH,$$

can be considered as butyric acid in which the end methyl group is converted into carboxyl. It occurs naturally in amber (*succinum*), hence its name, and is also found in certain fruit juices.

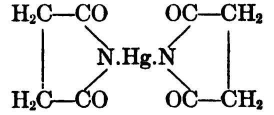
Succinic acid is a white crystalline body, used in medicine to a certain extent for rheumatism and bronchitis.

Dose.—0.3 to 1 Gm. (5 to 15 grains).

HYDRARGYRI SUCCINIMIDUM—Mercuric Succinimide

(Hydrarg. Succinim.)

$C_8H_8O_4N_2Hg$



Molecular weight, 396.69

Mercuric Succinimide contains, when dried for twenty-four hours over sulfuric acid, not less than 49.5 per cent and not more than 51 per cent of Hg, corresponding to not less than 98 per cent of $(CH_2CO)_2:NHgN:(COCH_2)_2$.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Small white crystals or white powder; odorless; stable in air but darkens in light; soluble in 20 parts of water and 5 parts of boiling water; slightly soluble in alcohol, insoluble in ether.

For *tests for identity*, for *impurities* (mercuric salts and chloride) and for *assay*, see U.S.P., p. 190.

Remarks.—This new official chemical is not an ordinary salt of mercury. As shown in the graphic formula given above, the mercury is bound to the nitrogen atoms of the two imido groups and not to the carboxyl groups of the usual organic acids. It is stated that unlike ordinary salts of mercury, its solutions are nonirritating, hence are useful for hypodermic injections. It is used as an antisyphilitic.

Dose.—0.015 Gm. (1/4 grain).

Malic acid,

$$COOH—CHOH—CH_2—COOH,$$

can be considered as monoxysuccinic acid, that is, succinic acid in which one hydrogen is replaced by hydroxyl. Malic acid was discovered in apples, *Pyrus malus*, by Scheele in 1785, and can be made synthetically from succinic acid. It is now prepared from maleic acid (p. 685). An amido derivative of succinic acid is *asparagin,*

$$CONH_2—CHNH_2—CH_2COOH,$$

which is found in many plants.

Malate of iron is sometimes used as a tonic. It is a constituent of *ferrated extract of apples* (N.F. V) which is made by treating reduced iron with fresh apple juice and then evaporating the resulting solution of crude ferrous malate to a pilular extract.

Tartaric acid,

$$COOH—CHOH—CHOH—COOH,$$

is dioxysuccinic acid, and was found by Scheele in 1769 in cream of tartar. It is interesting as being found in four distinct varieties, and more striking is that all of them seem to have the same graphic formula. The difference among these tartaric acids is chiefly their behavior toward polarized light, the one rotating the ray to the right, hence called dextrogyre, another rotating light to the left, or levogyre; a third does not deviate the ray of light at all, hence called inactive, and the fourth modification, which is also inactive, is racemic acid.

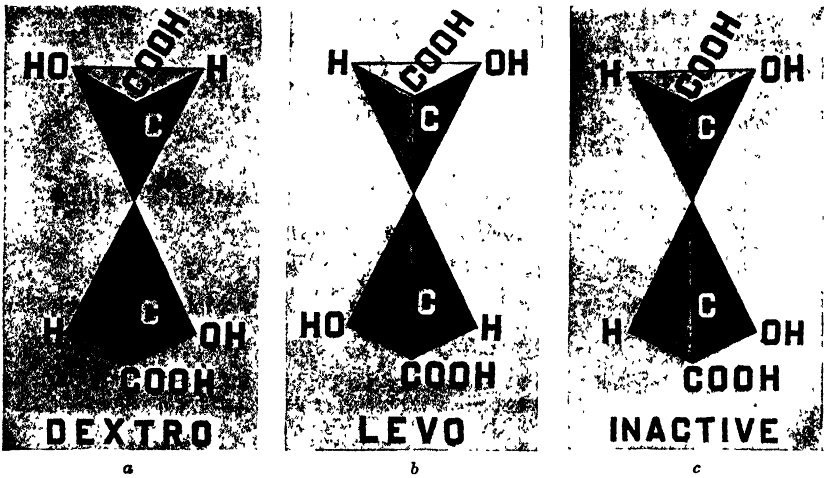


Fig. 268.—Tartaric acid formulas. *a*, Dextrogyrate; *b*, levogyrate; *c*, inactive.

The experiments of the three tartaric acids first mentioned, performed by Pasteur, have become classic, as constituting foundations of the theory of Van't Hoff: which is termed chemistry in space or *stereochemistry.*

Pasteur proved that the crystals of the dextrogyre tartaric acid and of the levogyre tartaric acid differ from each other only in the fact that one is the exact mirror picture of the other. He also proved that the inactive was a mixture of equal quantities of dextrogyre and levogyre tartaric acids.

Van't Hoff took up the study of the tartaric acids as opening a new field of thought. Up to this time chemical formulas were considered as simply pictures on flat surfaces, while his efforts were directed to attempt to show the exact location of the constituent atoms in a molecule, as to length, breadth, and thickness; thus producing a "space formula." It is, of course, far beyond the scope of this work to give any details of this fascinating theory, and the reader is, therefore, referred to Van't Hoff's book. Suffice it to say that Van't Hoff's theory is that the real difference among the three tartaric acids is merely the relative difference between the position of the hydrogen, hydroxyl, and carboxyl which they contain, and he gives the pictures (Fig. 268) of these three interesting bodies.

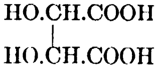
He also discovered a very interesting fact in regard to these bodies, namely, that each bond of the two central tetrahedral carbon atoms of the above pictures is attached to a different atomic grouping; thus one bond is attached to the other central carbon atom, another to a carboxyl, a third to a hydrogen, and a fourth to a hydroxyl. A carbon atom in which each bond is attached to different groups is called an *asymmetric carbon atom*, and is a constituent of all organic bodies which polarize light. This important statement was made some fifty years since and not only has never been disproved, but is now accepted as a fact. To understand this very striking chapter of chemistry thoroughly, a knowledge of crystallography and of polarization is essential, and as this is plainly beyond the limits of the present volume, the reader is advised to study the question in some standard work of physics.

The Fruit Acids include malic acid (from apples), tartaric acid (from grapes) and citric acid (from lemons). Nelson found that strawberries, pineapple, and red raspberries contain citric and malic acids, that black raspberries contain citric acid only and the Concord grapes contain malic and tartaric acids. It will be noticed that malic and tartaric acid are closely related. Weiss and Downs, by passing a mixture of benzene (p. 769) and air over a catalyst (vanadium oxide) heated between 400° and 450° C., have obtained maleic acid, COOH−CH=CH−COOH, and, from this, malic acid is now prepared upon a commercial scale.

ACIDUM TARTARICUM—Tartaric Acid

(Acid. Tart.)

$C_4H_6O_6$



$$\begin{array}{c}\text{HO.CH.COOH}\\ |\\ \text{HO.CH.COOH}\end{array}$$

Molecular weight, 150.05

Tartaric Acid contains not less than 99.5 per cent of $H_2C_4H_4O_6$.

Summarized Description.

Colorless, translucent, monoclinic prisms or fine white powder; acid taste; soluble in about 0.75 part of water, and in about 2.7 parts of alcohol; not more than $\frac{5}{100}$ of 1 per cent of ash. For details, see U.S.P., p. 30.

For *tests for identity*, for *impurities* (sulfate, oxalate, lead, heavy metals) and for *assay*, see U.S.P., p. 30.

Remarks.—The official tartaric acid, which is the dextrogyrate variety, occurs in the juice of grapes and in other fruit in the form of acid potassium tartrate, its commercial source being from *argol*, which represents the acid potassium tartrate which deposits from wine during the process of aging. The crude tartar or argol is cooked with chalk, thus forming calcium tartrate, which is then heated with sulfuric acid, forming insoluble calcium sulfate and soluble tartaric acid. A solution of the latter is then evaporated and crystallized.

Tartaric acid has also been prepared synthetically from maleic acid and from oxalic acid.

Tartaric acid is used as a refrigerant, especially in the form of potassium bitartrate. The acid is a constituent of the official *Seidlitz powders* and is interesting by reason of its ability to form three distinct classes of salts—normal, acid, and double. (See p. 400.)

PENTANE

(C_5H_{12})

The pentane derivatives of pharmaceutic interest are:

Amyl alcohols	$C_5H_{11}OH$.
Amyl nitrite, U.S.P.	$C_5H_{11}NO_2$.
Valerianic aldehyde	C_4H_9CHO.
Valerianic acids	C_4H_9COOH.

The halogen derivatives of pentane are of no pharmaceutic interest. The monatomic alcohols of pentane are not called pentyl alcohols, but go by the name of amyl alcohols, being so called because found abundantly in the spirit obtained by fermenting starch (amylum).

Amyl Alcohols ($C_5H_{11}OH$).—Eight isomeric forms of amyl alcohol are possible and all of these are known. These amyl alcohols are the chief constituents of *fusel oil.* (See p. 655.) Sharpless now recovers normal pentane from natural gas and converts it into amyl alcohol by the following procedure:

$$C_5H_{12} \rightarrow C_5H_{11}Cl \rightarrow C_5H_{11}OH$$

AMYLIS NITRIS—Amyl Nitrite

(Amyl. Nitris)

$C_5H_{11}NO_2$. Molecular weight, 117.09

Amyl Nitrite contains not less than 80 per cent of $C_5H_{11}ONO$.

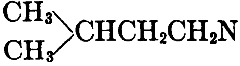
Storage.—Preserve in hermetically-sealed glass bulbs, or in tightly-stoppered vials, in a cool place and protected from light.

Summarized Description.

Clear yellowish liquid; ethereal fruity odor; pungent aromatic taste; almost insoluble in water; miscible with alcohol or ether: sp. gr. 0.865 to 0.875; very volatile; inflammable, burning with a yellow sooty flame. For details, see U.S.P., p. 56.

For *tests for identity,* for *impurities* (free acid, aldehyde) and for *assay,* see U.S.P., p. 56.

Remarks.—This ester, which is similar to ethyl nitrite (p. 662), is made by practically the same process as the former, namely, by treating amyl alcohol with potassium nitrite and sulfuric acid, and distilling the reaction product.

It can also be made by treating fusel oil or amyl alcohol with nitric acid and copper, the copper reducing the nitric acid to the nitrous form. This yields the official product, which consists of about 80 per cent of iso-amyl nitrite,  $\genfrac{}{}{0pt}{}{CH_3}{CH_3}\!\!>\!CHCH_2CH_2NO_2$, the rest being mixture of nitrites of the other amyl alcohols.

Amyl nitrite is a limpid, light yellow liquid, of pleasant but striking odor, and sharp taste. While it boils at 96° to 99° C., it is very volatile at ordinary temperatures, hence the preservation of amyl nitrite calls for considerable care, and the best form in which it can be put up is in sealed glass tubes rather than in glass-stoppered bottles.

Not merely is loss experienced in amyl nitrite by evaporation, but also by reason of the fact that in presence of moisture it decomposes into amyl alcohol and nitrous acid by the following reaction:

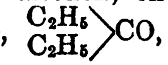
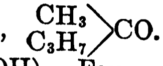
$$C_5H_{11}NO_2 + H_2O = C_5H_{11}\,OH + HNO_2;$$

hence in order to preserve amyl nitrite, it is necessary that it be kept absolutely dry. In the decomposition, crystals of ammonium tetroxalate have been known to form.

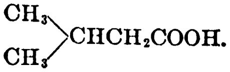
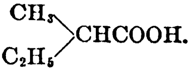
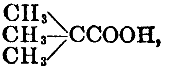
Amyl nitrite is a very valuable medicine, because it furnishes a specific in cases of suffocation resulting from attacks of angina pectoris. When sharp spells of this distressing complaint come on, the inhalation of amyl nitrite usually gives relief. Amyl nitrite is put up for this purpose in "*pearls*," that is, in small hollow shells of thin glass hermetically sealed. When the attack begins, the patient crushes one of these pearls in a handkerchief and inhales the escaping vapor.

Dose.—**By inhalation, 0.2 cc. (3 minims).**

Amyl Acetate may be made by treating amyl alcohol with acetic acid in the presence of sulfuric acid. It is a liquid of agreeable odor that is used as a solvent for nitrocellulose (p. 703).

The primary amyl alcohol on oxidation yields valerianic aldehyde, and this in turn yields valerianic acid. Secondary amyl alcohols, on the other hand, yield on oxidation either diethyl-ketone,  $\left.\begin{matrix}C_2H_5\\C_2H_5\end{matrix}\right>CO$, or methyl propyl ketone,  $\left.\begin{matrix}CH_3\\C_3H_7\end{matrix}\right>CO$.

Valeric Acid (C_4H_9COOH).—Four modifications of valeric acid are known:

Propyl acetic acid,	$C_3H_7CH_2COOH$.
Isopropyl acetic acid,	 $\left.\begin{matrix}CH_3\\CH_3\end{matrix}\right>CHCH_2COOH$.
Methyl ethyl acetic acid,	 $\left.\begin{matrix}CH_3\\C_2H_5\end{matrix}\right>CHCOOH$.
Trimethyl acetic acid,	 $\left.\begin{matrix}CH_3\\CH_3\\CH_3\end{matrix}\right>CCOOH$,

and of these, the one usually found in commerce is the isopropyl acetic acid, this body being recognized in pharmacy as *acidum valerianicum.*

Valerianic acid is a constituent of some animal fluids, such as sweat. It is also found in the form of esters in dolphin fat, but the chief natural origin of valerianic acid was from valerian root, from which it is obtained by distillation with water.

Usually, however, it is made by the oxidation of the appropriate amyl alcohol with potassium dichromate and sulfuric acid or by passing the vapor of the alcohol and air over copper gauze spirals heated to 370° to 390° C.

Valerianic acid is a mobile, oily liquid, boiling at 175° C., of specific gravity 0.935, having the characteristic odor of valerian. It combines with alkalis to form salts, such as the valerianates of ammonium, iron, and zinc, each of which is discussed under its respective metal, hence it is only necessary here to cite that, in order to get a white crystalline sample of ammonium valerianate, monohydrated valerianic acid must be used, and not the trihydrated frequently found in commerce. The trihydrated can be converted into the monohydrated by crystallizing a mixture of neutral sodium valerianate with the crude acid. and treating the crystalline acid salt with concentrated sulfuric acid.

Valine is alpha-amino-isovaleric acid, $(CH_3)_2CHCH(NH_2)COOH$. It is an active constituent of ergot. (See p. 941.)

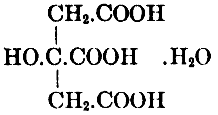
While tricarballylic acid, citric acid, and aconitic acid are derivatives of hexane, they can be most conveniently discussed in this chapter, leaving the next chapter for the sole consideration of those very important hexane derivatives, the carbohydrates.

Tricarballylic Acid ($C_3H_5(COOH)_3$).—This acid with the long name is cited not because of its pharmaceutic value, but merely because it is the connecting link between the compounds just mentioned and of the important organic acid which will be cited next. It will be seen, from the formula given below, that this represents that acid of hexane containing three carboxyls, and which, therefore, may be considered as the oxidation product of primary triatomic hexyl alcohol. It, therefore, serves the purpose of introducing its oxy-derivative, which is none other than *citric acid*, $C_3H_4OH(COOH)_3$.

ACIDUM CITRICUM—Citric Acid

(Acid. Cit.)

$C_6H_8O_7.H_2O$



$$\begin{array}{l} CH_2.COOH \\ \quad | \\ HO.C.COOH\ \ .H_2O \\ \quad | \\ CH_2.COOH \end{array}$$

Molecular weight, 210.08

Citric Acid contains not less than 99.5 per cent of $H_3C_6H_5O_7.H_2O$.
Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless, translucent crystals or white powder; soluble in about 0.5 part of water, in about 1.5 parts of alcohol and in 21 parts of ether. For details, see U.S.P., p. 18.

For *tests for identity*, for *impurities* (tartaric acid, oxalic acid, lead, sulfate, heavy metals, carbonizable impurities) and for *assay*, see U.S.P., p. 19.

Remarks.—Citric acid was isolated by Scheele in 1789 from the juice of lemon, and analyzed by Liebig in 1831; while its structure was proposed by Salet (1868) and confirmed by Grimaux and Adam (1880).

Citric acid occurs in the juice of the lemon and some other fruits; the former, however, being the source of the commercial article. By treating lemon juice with calcium carbonate, calcium citrate is precipitated out, and this precipitate, after being thoroughly washed, is treated with sulfuric acid, whereby a precipitate of calcium sulfate is formed and citric acid goes into solution. The citric acid solution is then concentrated in vacuo and allowed to crystallize.

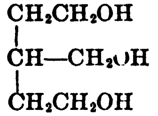
Several syntheses of citric acid have been accomplished, one of which is from carballylic acid, thus proving its structural formula. Fermentation processes of manufacture in which glucose is acted upon by special micro-organisms in the presence of a trace of nitrogenous matter, have been devised by Buchner and by other investigators. Several of these processes are now yielding citric acid in commercial quantities.

Citric acid occurs in translucent, right-rhombic prisms, melting at 152° to 153° C., having the specific gravity 1.6, and soluble in 0.5 part of water.

Citric acid crystallizes with 1 molecule of water of crystallization, and is prone to efflorescence. Moreover, if the acid is heated to 175° C., it will not merely lose its water of crystallization, but also a molecule of water from its own structural formula, with formation of a new body, *aconitic acid.*

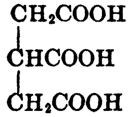
It may be well to compare the graphic formula of the three acids just mentioned along with the alcohol from which derived:

Primary triatomic hexyl alcohol.



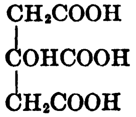
$$\begin{array}{l} CH_2CH_2OH \\ | \\ CH{-}CH_2OH \\ | \\ CH_2CH_2OH \end{array}$$

Tricarballylic acid.



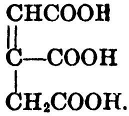
$$\begin{array}{l} CH_2COOH \\ | \\ CHCOOH \\ | \\ CH_2COOH \end{array}$$

Citric acid.



$$\begin{array}{l} CH_2COOH \\ | \\ COHCOOH \\ | \\ CH_2COOH \end{array}$$

Aconitic acid.



$$\begin{array}{l} CHCOOH \\ \| \\ C{-}COOH \\ | \\ CH_2COOH. \end{array}$$

The fact that citric acid easily parts with a molecule of water should always be borne in mind, and, therefore, undue heat should not be used in evaporating a solution of citric acid or of its salts. In fact, the evaporation should take place in vacuo.

DRUGS CONTAINING FRUIT ACIDS

In previous editions of this work, some attention was paid to the botanical side of pharmacy, at least as far as some salient botanical features of crude drugs were concerned. In this edition, however, the botanic side is omitted; first, in order to keep the book down to a reasonable size; secondly, since pure botany scarcely belongs in a book on pharmacy; and thirdly, as most pharmacy students of today have access to the admirable books on pharmaceutical botany such as those mentioned on pp. 15 and 16.

Vegetable drugs consist of whole plants, plant parts, or plant excretions, in other words, are portions of that collection of cells called a "plant." Knowledge of plants forms the science of botany, and a full discussion of this science is clearly beyond the limits of this work; hence the student is referred to list of standard textbooks given on pp. 15 and 16.

The study of vegetable drugs—of the plant parts used in medicine—forms that branch of knowledge called "organic materia medica," and even this in its complete form is beyond the province of this work. reference to the leading textbooks on the subject being found on pp. 15 and 16.

In the study of materia medica, drugs are usually grouped as belonging to the several classes of plant parts—roots, stems, rhizomes, tubers, woods, barks, leaves, bulbs, herbs, flowers, fruit, and seeds. For the meaning of these terms, the reader is referred to the botanical books mentioned on pp. 15 and 16.

Chemically, drugs consist of many substances; those that are plant organs consisting, histologically, of cell wall and cell contents, drugs that are exudations from plants being usually entirely cell contents. The cell wall, which consists of cellulose, wood, bast, or cork, according to its development is generally spoken of pharmaceutically as "*fibrous tissue.*" The cell contents consist of a vast number of bodies, such as alkaloids, glucosides, neutral principles, oils (volatile or fixed), tannin, resin, gum, starch, sugar, etc. The last four are found in almost all plants, while the others are more sparingly found, and constitute the active principle of the specific drug under consideration.

This leads to the classification of drugs into alkaloidal drugs, glucosidal drugs, astringent drugs, etc. In the consideration of every drug on the pages which follow the *constituents* will be an important feature study, and let it be here frankly stated that under constituents will be given only those which make the drug of value. Thus in considering alkaloidal drugs a continuous repetition of "gum, starch, and sugar" will be omitted, reference being made to these constituents only when they play an important rôle.

Rhus Glabra (U.S.P. X), or *Sumac Berries*, is the dried ripe fruit of *Rhus glabra*. It contains malates of potassium and calcium and also some tannin. It is used as a refrigerant and astringent. The infusion is used as a gargle in sore throat. *Dose.*—1 Gm. (15 grains).

Tamarindus (N.F. V), or *Tamarind*, is preserved pulp of the fruit of *Tamarindus indica* and is frequently found in commerce mixed with molasses.

Tamarinds are used as a refrigerant and laxative. A drink from tamarinds and cream of tartar is popular in the south for "thinning the blood."

Dose.—15 Gm. (240 grains).

Limonis Succus (U.S.P. VIII), or *Lemon Juice*, is the commercial source of citric acid. It contains citric acid (7 per cent), malic acid, sugar, pectin and gum. Note that the original "neutral mixture" (Mistura Potassii Citratis, p. 469) was made by neutralizing lemon juice with potassium bicarbonate. Lemon juice is a refrigerant and was formerly used on shipboard as a preventive of scurvy, a loathsome disease produced by a steady diet of salt meat. It is given in doses of 1 fluidounce.

Succus Citri (N.F. IV), or *Lime Juice,* is expressed from the lime fruit, *Citrus medica acida.* The nutritive value of both orange and lemon juice is now known to be due to their vitamin content. (See p. 955.)

Prunus Cerasus (N.F. VI), or *Sour Cherry,* is the fresh ripe fruit of cultivated varieties of *Prunus Cerasus.* It is the familiar fruit and has been made official only because of its use in making *syrup of cherry* N.F. (p. 223).

BIBLIOGRAPHY

Isopropyl Alcohol.—(Source) Anon., Yearbook A.Ph.A., 9, 1920, 513; Clough and John, Jl. Soc. Ch. Ind., 42, 1923, 1198A. (History and Tests) Leffmann and Pines, A.J.P., 102, 1930, 39. (Synthesis) Ed. Jl. Soc. Ch. Ind., 48, 1929, 126. (Uses and pharmacology) Heffter and Juckenack, Jl. Soc. Ch. Ind., 38, 1919, 924A; Anon., C.A., 15, 1921, 273; Grant, C.A., 16, 1922, 312; Macht, *ibid.,* 16, 1922, 2923; Fuller, C.A., 22, 1928, 2994; Bijlsma, C.A., 23, 1929, 3741.

Acetone.—(History) Liebig, A., 1, 1832, 223; Dumas, Ann. chim. phys., [2], 49, 1832, 208; Bridges, A.J.P., 10, 1838, 202. (Manufacture) Squibb, A.J.P., 67, 1895, 144 and Jl. Am. Ch. Soc., 18, 1896, 231; Jedlikca, C.A., 5, 1911, 2078; Appleyard, Jl. Soc. Ch. Ind., 42, 1923, 1236; Ardagh, Jl. Ind. Eng. Ch., 16, 1924, 1133; Gokhale, Jl. Soc. Ch. Ind., 44, 1925, 777B; Donath, Ch. Zt., 51, 1927, 924. (Reactions and tests) Meyer and Janny, B., 15, 1882, 1324; Tollens, B., 15, 1882, 1635; Grimm, A., 157, 1871, 262; Schaeffer, A.J.P., 98, 1926, 643; Zwikker, Ph. Weekbl., 67, 1930, 560. (Uses) Remler, Jl. Ind. Eng. Ch., 15, 1923, 717.

Sulfonal.—(Structure and pharmacology) Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 456. (Manufacture) Anon., Am. Dr., 18, 1889, 209. (Tests) Ritsert, Ph. Zt., 33, 1888, 312.

Trional.—Fromm, A., 253, 1889, 150; Spitzer, A.Ph.A., 41, 1893, 535.

Tetronal.—Baumann and Kast, Zt. physiol. Ch., 14, 1890, 64.

Mercaptan.—Diergart, C.A., 14, 1920, 935; Patterson, Jl. Soc. Ch. Ind., 43, 1924, 196.

Propionic Acid.—Gottlieb (1884), Beilstein, 1, 1893, 418; Sherman and Shaw, C.A., 18, 1924, 146.

Lactic Acid.—(Manufacture) Boutroux, A.Ph.A., 27, 1879, 460; Claflin, Jl. Soc. Ch. Ind., 16, 1897, 516; Allgeier, Jl. Ind. Eng. Ch., 21, 1929, 1039; Garret, *ibid.,* 22, 1930, 1153. (Tests) Arny and Dimler, Jl. A.Ph.A., 18, 1929, 459. (Uses) Anon., Ph. Jl., [3], 7, 1876, 116.

Bulgarian Bacillus.—Kühl, Yearbook, A.Ph.A., 59, 1911, 123; Puckner, Jl. A.M.A., 61, 1913, 2084; Carter, Jl. A.Ph.A., 8, 1919, 179; Anon., Jl. A.M.A., 73, 1919, 1887 and 1895; Olive, Ch. Met. Eng., 35, 1928, 616.

Glycerin.—(History) Pelouze, Ann. chim. pharm., 19, 1836, 210 and 20, 1837, 46; Wurz, Ann. chim. phys., [3], 43, 1855, 492; Robb, Ph. Jl., 107, 1921, 256; Darke and Lewis, Jl. Soc. Ch. Ind., 47, 1928, 1073; England, A.J.P., 104, 1932, 489. (Manufacture) Shinn, A.J.P., 22, 1850, 124; Carpenter, Jl. Soc. Ch. Ind., 2, 1883, 98; Shoemaker, Dr. Circ., 9, 1866, 7; Warner, A.Ph.A., 58, 1910, 341; Tilghman, U.S. Reports, No. 102, p. 707; Stendorf, Ap. Zt., 30, 1915, 500; Sandelin, Jl. Soc. Ch. Ind., 41, 1922, 769A; Sadtler, A.J.P., 95, 1923, 283; Schweizer and others, Yearbook, A.Ph.A., 8, 1919, 435. Tomada, Jl. Soc. Ch. Ind., 44, 1925, 185B; Penkovski, C.A., 23, 1929, 2240; Nishizawa and Inoue, C.A., 25, 1931, 6001. (Properties) Crookes, Ch. News, 15, 1867, 26; Bosart and Snoddy, Jl. Ind. Eng. Ch., 20, 1928, 1377; Harvey, Ph. Jl., 122, 1929, 376 and 415; Cocks, Jl. Soc. Ch. Ind., 48, 1929, 279T. (Antiseptic value) Goodrich, Ph. Jl., 98, 1917, 453. (Uses) Krantz, Jl. A.Ph.A., 12, 1923, 963.

Acrolein.—Hubner and Geuther, A.J.P., 32, 1860, 449; Senderens, Comp. rend., 151, 1910, 530; Bergh, Jl. prakt. Ch., 79, 1909, 351.

Nitroglycerin.—(History) Sobrero, Comp. rend. 24, 1847, 247, MacDonald, Arms and Explosives, 19, 1911, 60. (Manufacture) Gofner, Ch. Ind., 34, 1912, 307. (Properties) Monroe, Am. Dr., 17, 1888, 37; Darapsky, C.A., 1, 1907, 1059. (Pharmacology) Love and McGuigan, C.A., 20, 1926, 1851.

Glycerophosphates.—Robin, A.Ph.A., 42, 1894, 725; Rijn, C.A., 3, 1909, 357; Self, Ph. Jl., 80, 1908, 627; Dubois, Jl. Ind. Eng. Ch., 6, 1914, 122; Umney, Brit. Col. Dr., 1914, 69; Hegland, Ph. Week., 53, 1916, 1645; Bailly, C.A., 11, 1917, 331; Gilta, C.A., 21, 1927, 2205; Kogan, Ph. Cent., 69, 1928, 49; Hill and Pyman, Jl. Ch. Soc., 1929, 2236.

Boroglycerin.—McElhenie, A.J.P., 54, 1882, 352.

Chloretone.—Anon., Am. Dr., 36, 1900, 12; Anon., A.J.P., 79, 1907, 117; Hamilton, A.J.P., 91, 1919, 643.

Brometone.—Aldrich, Jl. Am. Ch. Soc., 33, 1911, 386.

Maleic Acid.—Weiss and Downs, Jl. Ind. Eng, Ch., 12, 1920, 228.

Butyl Alcohol.—(Manufacture) Thaysen, Jl. Soc. Ch. Ind., 45, 1926, 71; Bianchi, C.A., 24, 1930, 1457; Gabriel, Jl. Ind. Eng. Ch., 20, 1928, 1003 and 22, 1930, 1163; Walker, Jl. Soc. Ch. Ind., 49, 1930, 946.

Butyl Chloral Hydrate.—(Manufacture) Hofmann, Ph. Jl., [2], 11, 1870, 720; Kraemer and Pinner, A., 158, 1871, 37. (Properties) Mason, A.J.P., 46, 1874, 150. (Uses) Liebreich, Ph. Jl., [3], 6, 1876, 666.

Butyric Ether.—Rice, Am. Dr., 16, 1887, 9.

Banana Oil.—Anon., Merck's Rep., 15, 1906, 22.

Amber.—Tschirch, C.A., 17, 1923, 1644.

Succinic Acid.—Schmitt, A., 114, 1860, 106; Yardley, C.A., 18, 1924, 1929.

Fruit Acids.—Bigelow and Dunbar, Jl. Ind. Eng. Ch., 9, 1917, 762; Nelson, Jl. Am. Ch. Soc., 47, 1925, 568; *ibid.*, 47, 1925, 1177; *ibid.*, 52, 1930, 2928.

Malic Acid.—(History) Scheele (1785), Thorpe's Dict., 3, 1912, 380. (Structure) Schmitt, A., 114, 1860, 106. (Properties) Bancroft and Davis, C.A., 24, 1920, 3493. (Manufacture) Challenger, C.A., 25, 1931, 497.

Tinctura Ferri Pomata.—Oberhard, Ph. Zt., 74, 1929, 13.

Asparagin.—(History) Boutron-Chalard and Pelouze, Jl. de ph., 19, 1833, 208. (Structure) Dessaignes, A.J.P., 22, 1850, 245.

Tartaric Acid.—(History) Wootton, 1, 1910, 371; Arny, Am. Dr., 38, 1901, 3; X-rayser, Am. Dr., 58, 1911, 36; "S. M." Jl. Soc. Ch. Ind., 51, 1932, 317. (Structure) Liebig, A.J.P., 32, 1860, 347; Schmitt, A., 114, 1860, 106; Kolbe, A., 113, 1860, 317; Van't Hoff, Bull. soc. chim., [2], 23, 1875, 298; Longchambon, C.A., 20, 1926, 1594; Scheringa, C.A., 25, 1931, 4527; Amadori, C.A., 25, 1931, 4225. (Manufacture) Hölbing, Jl. Soc. Ch. Ind., 15, 1896, 712; Pasteur, A J.P., 25, 1853, 250; Dreyfus, Pharm. Era, 51, 1918, 76; Voss, C.A., 15, 1921, 2963. (Synthesis) Baekeland and Peter, Met. Ch. Eng., 15, 1916, 151; Dyson, Ch. and Dr., 116, 1932, 668. (Properties) Pasteur, Compt. rend., 35, 1852, 176; A.J.P., 26, 1854, 55.

Optical Rotation.—Fischer, B., 23, 1890, 371 and 40, 1907, 102; Sieg, Yearbook A.Ph.A., 5, 1916, 300.

Stereochemistry.—Van't Hoff, Bull. soc. ch., [2], 23, 1875, 298; Lowry, Jl. Soc. Ch. Ind., 43, 1924, 1048 and 46, 1927, 78 and 102; Delepine, Bull. soc. ch., 37, 1925, 197; Pope, *ibid.*, 44, 1925, 1225 and 51, 1932, 229T; Wedekind, Zt. angew. Ch., 43, 1930, 985.

Amyl Alcohols.—(Manufacture and properties) Cahours, A.J.P., 11, 1839, 260; Pasteur, A., 96, 1855, 255; Swenarton, Science, 70, 1929, 554. (Synthesis) Anon., Jl. Soc. Ch. Ind., 46, 1927, 770; Ayres, Jl. Ind. Eng. Ch., 21, 1929, 899; Armstrong, Jl. Soc. Ch. Ind., 49, 1930, 178.

Amyl Nitrite.—(Manufacture) Maisch, A.J.P., 43, 1871, 146; Nietsch, A.Ph.A., 29, 1881, 299. (Properties) Taylor, Jl. A.Ph.A., 3, 1914, 1327. (Pharmacology) Love and McGuigan, C.A., 20, 1926, 1851. (Uses) Anon., Dr. Circ., 14, 1870, 189. (Decomposition) Sandquist and Mohlin, Ph. Cent., 61, 1920, 371 and 455. (Pearls) Markwell, Ph. Jl., 121, 1928, 124.

Valeric Acids.—(History) Trommsdorf, A.J.P., 6, 1834, 351. (Manufacture) Dumas and Stass, A., 35, 1840, 145; Duclaux, Am. Dr., 16, 1887, 169; Mossler, Ph. Jl., 86, 1911, 175; Stahlmann, A.Ph.A., 17, 1869, 248; Piotrowski, Jl. Soc. Ch. Ind., 48, 1929, 934B. (Properties) Erlenmeyer and Hell, A., 160, 1871, 264; Schmitt and Sachleben, A., 193, 1878, 87; Hager, A.J.P., 52, 1880, 134.

Valine.—Clark and Fittig, A., 139, 1866, 199.

Tricarballylic and Aconitic Acids.—Pawolleck, A., 178, 1875, 153 and 167; Malachowski, C.A., 23, 1929, 1878.

Citric Acid.—(History) Grimaux and Adam, Comp. rend., 90, 1880, 1252. (Manufacture) Flückiger, Arch. d. Pharm., 227, 1899, 1065; Wilson, J. Ind. Eng. Ch., 13, 1921, 554; Warneford and Hardy, Jl. Ind. Eng. Ch., 17, 1925, 1283; Melis, Jl. Soc. Ch. Ind., 45, 1926, 690B. (Production by fermentation) Buchner and Wüsterfeld, C.A., 3, 1909, 1994; Martin, A.J.P., 88, 1916, 337; Molliard, J. ph. ch., 19, 1919, 317; Ganassini, C.A., 15, 1921, 2525; Starck, Pract. Dr., 47, Dec., 1929, 64; Challenger, C.A., 23, 1929, 377; Virtanen and Pulkki, C.A., 25, 1931, 4299; May and Herrick, C.A., 26, 1932, 4906. (Properties) Perciabosco, C.A., 25, 1931, 1219. (Tests) Arreguine, C.A., 23, 1929, 4166.

Rhus Glabra.—Rogers, A.J.P., 7, 1835, 56; Watson, A.J.P., 25, 1853, 193; Peacock, A.J.P., 97, 1925, 471.

Tamarinds.—Mueller, Ph. Cent., 23, 1887, 581 and 593.

Lemon Juice.—Borntraeger, A.Ph.A., 46, 1898, 719; Huerre, Jl. ph. Ch., 20, 1919, 5; Zilva, C.A., 18, 1924, 3411; Matlack, A.J.P., 100, 1928, 243; Editorial, Jl. Soc. Ch. Ind., 47, 1928, 909; Levi, C.A., 24, 1930, 893; Supple and King, Jl. Am. Ch. Soc., 52, 1930, 420; Joslyn and March, C.A., 25, 1931, 1293; Melis, C.A., 25, 1931, 4358.

Orange Juice.—Byfield, Daniels and Loughlin, C.A., 14, 1920, 3450.

CHAPTER XXXIX

DERIVATIVES OF HEXANE

THE following derivatives of hexane (C_6H_{14}) are of interest:

Hexyl alcohols	$C_6H_{13}OH$.
Capronic acid	$C_5H_{11}COOH$.
Gluconic acid	$CH_2OH(CHOH)_4COOH$.
Mannitol Dulcitol Sorbitol	$C_6H_8(OH)_6$.
Dextrose, U.S.P.	$C_6H_{12}O_6$.
Glucose, U.S.P.	Dextrose, maltose, dextrins, etc
Sucrose, U.S.P.	$C_{12}H_{22}O_{11}$.
Lactose, U.S.P.	$C_{12}H_{22}O_{11}.H_2O$.
Starch, U.S.P.	$(C_6H_{10}O_5)x$.
Gums	$C_6H_{10}O_5$.
Cellulose (purified cotton, U.S.P.)	$(C_6H_{10}O_5)x$.
Pyroxylin, U.S.P.	Chiefly $C_{12}H_{16}(ONO_2)_4O_6$.
Glucosides.	
Tricarballylic acid	$C_3H_5(COOH)_3$.
Citric acid, U.S.P.	$C_3H_4(OH)(COOH)_3$.

Of the *hexyl alcohols*, seventeen are possible, but since none are of pharmaceutic value, they will not be discussed.

By the oxidation of one of these alcohols, *capronic acid*, $CH_3(CH_2)_4$-COOH, is obtained. This capronic acid is a fatty acid discovered by Chevreul in 1824, and is found as an ester in coconut oil, Limburger cheese, and goat butter, and is cited merely because it is the only monobasic acid of hexane of pharmaceutic interest.

Mannitol, $C_6H_8(OH)_6$, is the hexatomic alcohol of hexane. It was isolated by Proust from manna in 1806, and is also found in minute traces in other drugs. The chief source of commercial mannite is manna, from which it is obtained by treating with boiling alcohol. From the alcoholic solution the mannite separates on cooling in small white crystals of sweetish taste.

Mannitol is now made commercially by direct crystallization from a purified aqueous solution of manna.

Dulcite and *sorbite* are isomeres of mannite, the former obtained by reduction of lactose (milk sugar) and the latter by reduction of glucose.

The three hexatomic alcohols mentioned above, mannitol, sorbitol, and dulcitol, yield ketone and aldehyde derivatives which are of great importance, such as *glucose, mannose, sucrose, starch,* and *cellulose.*

The formula of the first two is $C_6H_{12}O_6$.

Sucrose is $C_{12}H_{22}O_{11}$, while starch and cellulose are $(C_6H_{10}O_5)x$.

On examining these formulas it will be noticed that the hydrogen and oxygen atoms attached to the carbon atoms are present in exactly the same proportion as in water, viz., there are always twice as many hydrogen atoms as oxygen atoms. For this reason to this class of bodies was assigned the name "*carbohydrates,*" although at present but little stress is laid on this characteristic.

Carbohydrates.—While most carbohydrates are derivatives of hexane, some are found containing more or less carbon than six. Thus, arabinose is $C_5H_{10}O_5$. On the other hand, some contain seven carbon atoms, some eight carbon atoms, and some nine; but practically all well-known carbohydrates are derivatives of hexane.

The hexane carbohydrates can be roughly grouped into three classes, the first having the form $C_6H_{12}O_6$, which have representatives in glucose and dextrose; the second, being of double formula, $C_{12}H_{22}O_{11}$, is found in cane sugar; while the group $C_6H_{10}O_5$ has representatives in such well-known bodies as starch, gum, and cellulose.

The first examination of these bodies shows that one should be derived from the other, thus:

$2C_6H_{10}O_5$, which is	$C_{12}H_{20}O_{10}$
plus one molecule of water,	H_2O,
gives us a molecule of sugar	$C_{12}H_{22}O_{11}$,
and when to this we add another molecule of water,	H_2O,
we get	$C_{12}H_{24}O_{12}$
or	$2C_6H_{12}O_6$,
which is the formula of glucose.	

The transition of starch or sugar into glucose is readily performed by the adding of water (by chemical means). The reverse operation is not so simple a one, and has been only recently performed.

It may be as well to state right here that the agent used for the molecular addition of water is usually a diluted sulfuric acid, and the process of chemically combining water is called "*hydrolyzing.*" On the other hand, if it is desired to remove water from the molecule of an organic substance, concentrated sulfuric acid is usually the agent employed, when it is said to act as a "*dehydrator.*"

The formula, $C_6H_{12}O_6$, it will be noticed, differs from the formula of mannitol, $C_6H_{14}O_6$, by containing 2 atoms of hydrogen less. It will be also noticed that this is the difference between the formula of an ordinary alcohol and its aldehyde or ketone, and it is really true that $C_6H_{12}O_6$ is an aldehyde or ketone derivative of the hexatomic alcohol, $C_6H_8(OH)_6$. The carbohydrates are called *aldoses*, or *ketoses*, according as the alcohol group has been changed to an aldehyde or a ketone, though some are of more intricate composition.

The carbohydrates can best be studied by taking up three groups in their regular order, viz.:

Those having formula $C_6H_{12}O_6$, or monosaccharides (monoses).
$C_{12}H_{22}O_{11}$, or disaccharides (bioses).
$(C_6H_{10}O_5)x$, or polysaccharides.

THE MONOSACCHARIDES
($C_6H_{12}O_6$)

These are bodies of more or less sweetness, and all possess optical activity, that is, all deviate the ray of polarized light either to right or left, except the synthetic inactive varieties. According to van't Hoff's rule, each active substance should contain at least one asymmetric carbon atom, and investigation has shown that this is true in every case. Several syntheses of these bodies have been accomplished; thus paraformaldehyde cooked with milk of lime gives acrose; formaldehyde cooked with milk of lime gives a mixture of formose and acrose (p. 650). Likewise dibromide of acrolein (p. 679), when treated with barium hydroxide, gives acrose. The bodies of this series are all readily converted into alcohol when brought into contact with yeast. If other bacteria of fermentation are added, they yield lactic or butyric acid or dextrin, as the case may be.

Following the rule of aldehydes and alcohols, these bodies of formula $C_6H_{12}O_6$ oxidize to special acids under treatment, and, on the other hand, can be reduced to special alcohols.

They all combine with calcium or strontium to form alcoholates of the same. They give all the reactions characteristic of aldehydes and ketones, for example, form distinct crystalline bodies with phenyl hydrazine. Some bodies of the group (mannose, galactose, and glucose) oxidize to the corresponding acid, thus showing aldehyde characteristics, while the fructoses, under similar treatment, break up, thus showing their ketone characteristics.

The bodies of formula $C_6H_{12}O_6$ can be roughly divided into two groups:

Fructoses, $CH_2OH—(CHOH)_3—CO—CH_2OH$.
Mannoses, galactoses, and glucoses, $CH_2OH—(CHOH)_4—CHO$.

Of each of these, three varieties are known: (1) the levogyre, which rotate the ray of light to the left; (2) the dextrogyre, which rotate the ray to the right; and (3) the inactive, which do not affect the ray of light.

It will be noticed that levogyre is abbreviated to the letter "l," dextrogyre, to "d," and inactive, to "i," and let it be stated here that in future, in this work, these abbreviations will be used instead of the long technical names.

Of the three *fructoses*, the dextrogyre variety (*fruit sugar* or *levulose*) is the sweet constituent of many fruits. It is now produced on a commercial scale from the root of Jerusalem artichoke (*Helianthus tuberosus*).

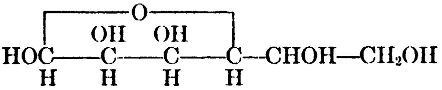
The three *mannoses* are of no pharmaceutic interest except as derivatives of mannite.

The three *galactoses* are of no pharmaceutic interest except from the fact that the dextrogyrate variety is a hydrolysis product of lactose (pages 696 and 700).

The work of Haworth and others during recent years has changed our views as to the structure of carbohydrates. Haworth's views may be summarized as follows:

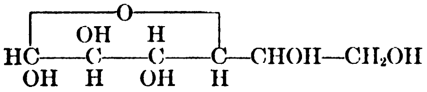
1. These carbohydrates may exist in two modifications: the *alpha* and the *beta* forms.
2. The structural difference may be shown by printing the graphic formulæ for the two types of glucose;

Alpha-glucose



$$\begin{array}{lllll} \multicolumn{4}{c}{\overbrace{\hspace{9em}}^{O}} & \\ & OH & OH & & \\ HOC— & —C— & —C— & —C & —CHOH—CH_2OH \\ H & H & H & H & \end{array}$$

Beta-glucose

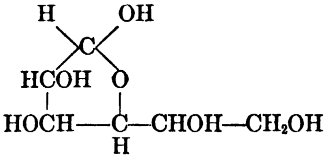


$$\begin{array}{lllll} \multicolumn{4}{c}{\overbrace{\hspace{9em}}^{O}} & \\ & OH & H & & \\ HC— & —C— & —C— & —C & —CHOH—CH_2OH \\ OH & H & OH & H & \end{array}$$

These, it will be noticed, differ only on the relative arrangement of the hydrogen atom and of the hydroxyl group on certain of the carbon atoms.

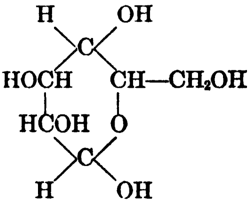
3. Haworth also suggests as possible structures for the two glucose molecules the following:

Alpha-glucose



The ringed portion of this formula is called the *furanose* ring.

Beta-glucose



The ringed portion of this formula is called the *pyranose* ring.

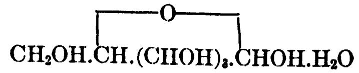
4. Similar formulæ of either the furanose or pyranose type have been devised for mannose, fructose, and galactose.

Of the three *glucoses* the only one of interest is the dextrogyrate variety, dextrose.

DEXTROSUM—Dextrose

(Dextros.—*d*-Glucose)

$C_6H_{12}O_6.H_2O$



$CH_2OH.\overbrace{CH.(CHOH)_3.CH}^{O}OH.H_2O$

Molecular weight, 198.11

A sugar usually obtained by the hydrolysis of starch.

Storage.—Preserve in well-closed containers.

Summarized Description.

White crystalline powder or granules; odorless; sweet taste; soluble in 1 part of water and in 48 parts of alcohol; more soluble in boiling water and boiling alcohol; $[\alpha]_D = +52.5°$ to $+53°$.

For details, see U.S.P., p. 134.

For *tests for identity* and for *impurities* (dextrin, soluble starch, sulfite, chloride, sulfate, heavy metals, arsenic), see U.S.P., p. 135.

Remarks.—This pure carbohydrate has been admitted to the body of the present Pharmacopœia because of its use as a readily absorbed food.

GLUCOSUM—Glucose

(Glucos.—Liquid Glucose)

A product obtained by the incomplete hydrolysis of starch. It consists chiefly of dextrose (*d*-glucose, $C_6H_{12}O_6$), maltose, dextrins, and water.

Summarized Description.

Colorless or slightly colored thick syrupy liquid; sweet taste; very soluble in water; sparingly soluble in alcohol. For details, see U.S.P., p. 179.

For *tests for identity* and for *impurities* (water, free acid, starch, sulfur dioxide, heavy metals, arsenic), see U.S.P., p. 179.

Remarks.—This product is one of the constituents of honey (which see), and can be made by inversion (hydrolysis) of cane sugar and of starch, the reaction being as given on p. 693. The commercial source of glucose is corn, from which the embryo is removed by mechanical means, the residue treated with sodium hydroxide to remove gluten and albuminous matter naturally found in the corn, and the starch thus purified is then hydrolyzed by treating with a diluted hydrochloric acid. On completion of the inversion, the aqueous solution of glucose is concentrated in vacuo. It is interesting to note that the separated embryo of the corn, when submitted to expression, yields a considerable quantity of fixed oil (*corn oil*), which is a valuable drying oil. The original intent of removing the germ was to prevent the glucose liquid from being greasy, and this affords another instance of the development of a special industry by the utilization of side products. Glucose is a thick, syrupy liquid, having specific gravity 1.412, perfectly miscible with alcohol and water. Glucose is a reducing agent, changing cupric salts to the cuprous form. Just as sulfuric oxide, SO_3, can be converted into sulfurous oxide, SO_2, by reduction, so can cupric oxide, CuO (or its hydroxide, dissolved in excess of alkali), be reduced to cuprous oxide, Cu_2O, as shown below:

$$\begin{array}{lcl} & 2CuO = & Cu_2O_2 \text{ cupric oxide} \\ \text{less} & & \underline{\quad O \quad} \\ & \text{yields} & Cu_2O \text{ cuprous oxide,} \end{array}$$

the valence of the copper being reduced during the reaction from II to I.

While this reaction occurs under the influence of any reducing agent, it is usually confined to the identification and estimation of glucose, for which it is admirably adapted, the brick-red precipitate of cuprous oxide being very characteristic. Glucose is a constituent of urine in diabetes, and in this way its identification is of much importance to the pharmacist. In examining the urine for sugar either Fehling's or Trommer's test is applied. The latter, which is the oldest, consists in treating the suspected urine with a solution of copper sulfate and a few drops of solution of soda (whereby the copper sulfate is converted into cupric hydroxide). On boiling, this blue cupric hydroxide is converted into brick-red cuprous oxide if glucose or other reducing agent be present.

Fehling's solution is an improved modification intended for volumetric analysis. It contains sodium and potassium tartrate (Rochelle salt), in addition to copper sulfate and sodium hydroxide. It is found among the volumetric solutions of the Pharmacopœia. (See Part V.)

Galactose ($CH_2OH(CHOH)_4CHO$).—This monose is made by inversion of milk sugar. It oxidizes to mucic acid, and is of no pharmaceutic value.

Mucic Acid, $COOH—(CHOH)_4COOH$, is now made commercially from scrap larch wood. Being a dibasic acid it can be used in place of the more expensive tartaric acid in such pharmaceutical preparations as effervescent salts.

Gluconic acid, $CH_2OH(CHOH)_4COOH$, is obtained by the oxidation of glucose with bromine. Calcium gluconate (below) is now largely prescribed as a soluble tasteless, nonirritating salt that may be administered, orally, intravenously or intramuscularly, in calcium therapy.

CALCII GLUCONAS—Calcium Gluconate

(Calc. Glucon.)

$C_{12}H_{22}O_{14}Ca.H_2O$ $[CH_2OH(CHOH)_4.COO]_2Ca.H_2O$. Molecular weight, 448.27

Calcium Gluconate is the normal calcium salt of gluconic acid. It yields not less than 12.4 per cent and not more than 12.8 per cent of CaO.

Storage.—Preserve in well-closed containers.

Summarized Description.

White crystalline or granular powder; odorless and tasteless; soluble in about 30 parts of water and in 5 parts of boiling water; insoluble in alcohol and ethereal solvents.

For *tests for identity,* for *impurities* (dextrose, sucrose, chloride, sulfate, heavy metals and arsenic) and for *assay,* see U.S.P., p. 99.

Remarks.—As mentioned above, calcium gluconate is used to obtain the therapeutic effects of calcium. It is more palatable than calcium chloride for oral administration and is nonirritating when given hypodermically or intramuscularly.

Dose.—Oral, 5 Gm. (75 grains). Intravenous, 1 Gm. (15 grains).

THE DISACCHARIDES

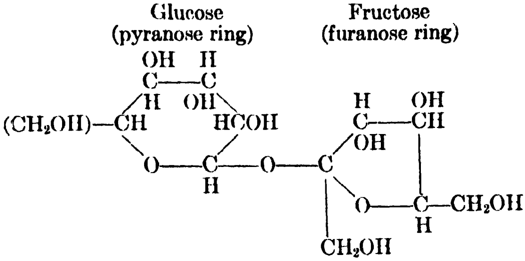
$(C_{12}H_{22}O_{11})$

The bioses are those carbohydrates having the formula $C_{12}H_{22}O_{11}$, and, as mentioned above, these represent two molecules of $C_6H_{12}O_6$ minus one molecule of water. They are much more easily crystallized than the monoses, are optically active, and are fermentable only after being hydrolyzed, the sole exception to this statement being that maltose is directly fermentable. As already mentioned, the bioses, under treatment with dilute sulfuric acid and special ferments, such as diastase, are hydrolyzed into bodies having the formula $C_6H_{12}O_6$. Each biose yields different products under hydrolysis; thus cane sugar hydrolyzes to glucose and fructose; maltose to glucose; lactose to galactose and glucose.

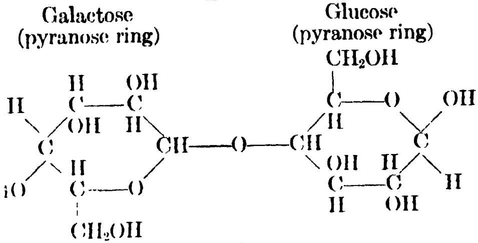
Maltose and lactose reduce silver nitrate and Fehling's solution, hence are aldehydes. Cane sugar, on the other hand, does not act in this way, hence contains no aldehyde groups. All three of these bioses form esters of acetic acid containing eight acetyl groups, from which is deduced the fact that each contains eight hydroxyls. There is much in the chemistry of these bodies yet to be cleared, but from the few facts already mentioned it has been decided that they represent anhydrides of the various glucoses, evidently those into which they separate under hydrolysis.

The exact graphic formulas of these bodies are still uncertain; but Haworth suggests the following:

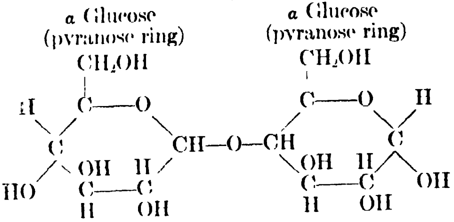
Sucrose



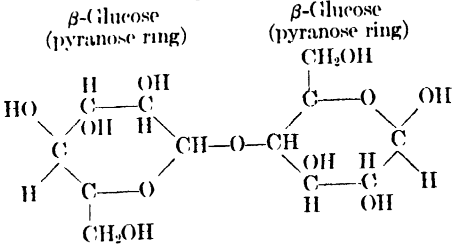
Lactose



Maltose

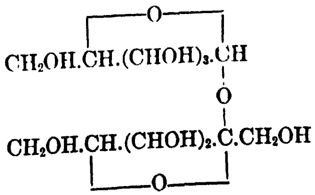


Cellobiose



SUCROSUM—Sucrose

(Sucros.—Saccharum, Sugar)



$$\begin{array}{c} \overbrace{CH_2OH.CH.(CHOH)_3.CH}^{O} \\ | \\ O \\ | \\ \underbrace{CH_2OH.CH.(CHOH)_2.C.CH_2OH}_{O} \end{array}$$

$C_{12}H_{22}O_{11}$

Molecular weight, 342.17

A sugar obtained from *Saccharum officinarum* Linné (Fam. *Gramineæ*), *Beta maritima* Linné (Fam. *Chenopodiaceæ*), and other sources.

Summarized Description.

White, hard, dry crystals or white crystalline powder; sweet taste; soluble in about 0.5 parts of water, in about 137 parts of alcohol; insoluble in chloroform or ether; aqueous solution is dextrorotatory; $[\alpha]_D = +65.9°$. For details, see U.S.P., p. 365.

For *tests for identity* and for *impurities* (insoluble salts, ultramarine or Prussian blue, invert sugar, calcium, heavy metals, sulfate and chloride), see U.S.P., p. 365.

Remarks.—Sucrose or *cane sugar* is obtained from cane, *Saccharum officinarum,* or from beet, *Beta maritima,* the products in each case being chemically identical. The two varieties of commercial sugar are yielded by two distinct plants. The sugar cane closely resembles the corn plant and in preparing sugar the stalk is cut near the roots at the proper season, the leaves lopped off from the stalks, which are then passed through rollers, by which means the juice is expressed. The juice is treated with lime to remove the gluten and albumin, followed by sulfur dioxide and the lime is finally removed either as calcium carbonate or phosphate. This treatment removes gluten and albumin and renders the filtered juice less liable to fermentation when the liquid consists of a thin solution from which sugar is obtained by appropriate concentration. Formerly the filtered juice was concentrated in large pans under atmospheric pressure ("open kettle process"). In such cases, however, the solution underwent slight decomposition, darkening the product, and forming the commercial brown sugar. To refine this brown sugar it is necessary to redissolve and clarify it with albuminous matter, such as blood, filter through charcoal and the solution concentrated in vacuo, and at the present time this concentration in vacuo is done from the very beginning. When the liquid in the vacuum pan has reached a proper degree of concentration, and the sugar is beginning to separate out by crystallization, the mass is transferred to centrifugal machines and is thus freed from moisture.

The process of making beet sugar is more complicated than that of making cane sugar, the saccharine solution being prepared by chopping the beets into small particles and macerating same in warm water, this process being known as the diffusion process. This solution contains many more impurities than does the cane juice, hence several methods of purification have to be used, and in this way quite a number of side products of more or less value are obtained. Thus, it will be recalled that methyl chloride (p. 645) is now obtained largely from beet sugar residue.

The process of diffusion mentioned above is now used in some factories in the manufacture of cane sugar. The cane, instead of being run through rollers, is relieved of its sugar by maceration in warm water. The extraction in this case is much more thorough than by pressure, but requires more manipulation, making the process more expensive.

The sucrose obtained by the methods just described is in the form of straw-colored granules and has to be further purified in central sugar refineries.

The synthesis of sucrose from the tetracetates of glucose and of gamma-fructose was accomplished by Pictet and Vogel in 1928.

Sucrose appears in commerce usually in the granulated form, although in some sections of the world the old-fashioned sugar loaf is still used. This is made by pouring a highly concentrated warm solution of sucrose into conical molds, letting stand twenty-four hours, draining off the syrup, and drying.

If a saccharine solution is allowed slowly to crystallize on strings, large transparent crystals are formed, these being known as *rock candy*. Sucrose melts at 160° C., and if the sucrose which has been brought to the melting point with the aid of a little water is then allowed suddenly to cool, it produces a candy form of sucrose sometimes called *barley sugar*. If sucrose is heated to 200° C., the product begins to carbonize and results in a deep brown liquid called *caramel*. This liquid is used largely as a coloring matter in soda-water syrups: hence it will not be amiss to outline method of preparation. Thus, if the carameled sucrose is allowed to cool without addition of water, it will thicken to a difficultly soluble mass. The addition of cold water to the highly heated fused mass causes the sudden evolution of steam, with a sputtering which may be dangerous when manufacturing caramel; hence to insure perfect results, to the caramelized sucrose at the proper stage should be added boiling water and not cold water. *Caramel* is recognized in the National Formulary. Commercial caramel is made to attain a darker tint by adding to the sucrose (or glucose), during heating, such chemicals as ammonium sulfate and hydrochloric acid, ammonium carbonate or sodium acetate.

In making sucrose by the open kettle process there is obtained a large amount of brown mother liquor, and this contains a quantity of sucrose in uncrystallized form, and the concentrated product is called *molasses*. In the modern manufacture of sucrose the aim is to make as large an amount of sucrose as possible, and therefore results in a corresponding loss in the yield of molasses. In the vacuum pan sugar-making the amount of molasses produced is very small, and even from this the sucrose is extracted by treatment with strontium salts (which form soluble strontium saccharate), from which the sugar can be eventually isolated in crystalline form. Barium salts have also been used for this purpose.

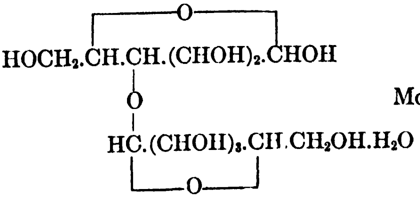
Sucrose, U.S.P., is a white, crystalline solid, of specific gravity 1.340, and soluble in 0.5 part of cold water, and sparingly soluble in alcohol. When treated with concentrated sulfuric acid the water is extracted, leaving carbon behind, in other words, sulfuric acid carbonizes sugar. Its saturated aqueous solution forms *syrup*, U.S.P. Sucrose is chiefly used as a sweetener, possessing in this way decided nutritive properties.

The relative sweetness of sugars is classified according to Martindale as follows: sucrose, 100; levulose, 173; glucose, 71; maltose, 32; galactose, 32; lactose, 16.

Maple Sugar is obtained by evaporating the spring sap of *Acer saccharum* and a few other species of maple. Besides sucrose, maple sugar contains small amounts of malic and other acids as well as its distinctive flavor. It is a popular form of candy.

LACTOSUM—Lactose

(Lactos.—Saccharum Lactis, Milk Sugar)



$$HOCH_2.CH.CH.(CHOH)_2.CHOH \quad O \quad HC.(CHOH)_3.CH.CH_2OH.H_2O$$

$C_{12}H_{22}O_{11}.H_2O$ Molecular weight, 360.19

A sugar obtained from milk.

Storage.—Preserve in well-closed containers.

Summarized Description.

Hard, white, crystalline masses, or white powder; faintly sweet taste; soluble in about 4.9 parts of water and in 2.6 parts of boiling water; almost insoluble in alcohol;

insoluble in chloroform or ether; aqueous solution is dextrorotary; $[\alpha]_D = 52.2°$ to 52.5°. For details, see U.S.P., p. 199.

For *tests for identity* and for *impurities* (dextrin, dextrose, sucrose, starch, heavy metals), see U.S.P., p. 200.

Remarks.—Just as our old friend, sugar, is now preening as *sucrose* U.S.P. (p. 697) even so infants will now have to call for *lactose,* when they want sugar of milk for their modified milk; since U.S.P. X and XI have adopted "Lactosum" and "Lactose" for the official names of this carbohydrate.

Lactose is a normal constituent of milk. Up to 1900, practically all milk sugar was made in Switzerland, since in the United States, the whey obtained in cheese manufacture was used to feed cattle. At present, however, much sugar of milk is made in this country, most of it being produced in New York State.

Milk sugar is made in Switzerland by simple concentration of whey in open kettles and then crystallizing on sticks. In this country the whey is evaporated in vacuo, and the moist granular mass dried in a centrifugal machine.

Milk sugar appears either in hard white crystals or in fine white powder, with a taste not so sweet as that of cane sugar. It directly reduces Fehling's solution, while cane sugar has no action on Fehling's solution until hydrolyzed. Another point of chemical distinction between the two products is shown in the test of a former Pharmacopœia, namely, that milk sugar when sprinkled upon concentrated sulfuric acid should not blacken the same; if it did, the presence of cane sugar is indicated. In carrying out this test great care should be exerted to use nothing but the pure powdered milk sugar. If fragments of the stick or string on which it crystallized were present, such would produce a brown color with the acid.

The synthesis of lactose from beta-galactose and beta-glucose was accomplished in 1927 by Pictet and Vogel.

Commercial lactose consists of a mixture of alpha and beta varieties (see p. 697.) *Beta lactose* is much more soluble than alpha lactose and has other advantages. It may be obtained practically free from the alpha variety by heating a solution of commercial lactose in a suitable autoclave at 93° C. Beta lactose is now an article of commerce.

Maltose is the sugar which is found in official *malt.* Malt is made from barley by placing same in a warm, moist, light place, and when the seeds begin to sprout, they are heated sufficiently to destroy the life of the young plants. The sprouting of a seed means the gradual development of embryo found therein, and during the first stages of its development the starch which is stored up in the seed serves for its food until there is developed a sufficient number of leaves to generate its own food from the carbon dioxide of the air. The starch which is found in the seed has to be converted into soluble forms before it can be assimilated by the embryo, and in the case of barley, it is converted into maltose by the action of the ferment *diastase* naturally residing in the seed. In manufacturing malt from barley the latter is allowed to grow until practically all the starch has been converted into maltose by the diastase. Maltose is of interest as the sugar constituent of *extract of malt* (p. 301).

It is now available in commercial quantities.

Cellobiose has been whimsically described as "the disaccharide of filter paper." It is isomeric with maltose but differs from it in optical activity.

The recent formulas suggested for starch and for cellulose express groupings of the pyranose rings and are very complicated, the simplest expressing at least four such rings. According to Pictet, soluble starch must represent at least 18 $C_6H_{10}O_5$ groups.

THE POLYSACCHARIDES

$(C_6H_{10}O_5)x$

These furnish several well-known products, both cellulose and starch being examples. While it is convenient to assign to these the simple $C_6H_{10}O_5$ formula it is a well-known fact that the individual molecules contain more than six carbon atoms; hence the "x" added to the formula given above.

Cellulose is so called because it represents the coating of the cell. Living cells consist primarily of a semiliquid portion called the protoplasm and nucleus surrounded by a cell wall, and this cell wall, when in a state of the greatest purity, consists of pure cellulose. A striking illustration of pure cellulose in the form of cell wall is found in the official *cotton*, which consists of the hairs of the seed of *Gossypium herbaceum*. In this case each hair consists of a single emptied cell, hence it is nothing but a cell wall, and this, on chemical analysis, is shown to be pure cellulose.

Cotton consists of long filaments, insoluble in water, alcohol, and ether, but soluble in ammoniacal solution of copper oxide (not ammoniacal solution of copper sulfate, as stated in some books). Cotton is used solely for mechanical purposes, and is of great value in pharmacy for such operations as filtering and straining, and in surgery as a dressing. The general use of cotton in the form of cloth is too well known to need remark.

GOSSYPIUM PURIFICATUM—Purified Cotton

(Gossyp. Purif.—Absorbent Cotton)

The hairs of the seed of cultivated varieties of *Gossypium herbaceum* Linné, or of other species of *Gossypnum* (Fam. *Malvaceæ*), freed from adhering impurities and linters, and deprived of fatty matter.

Summarized Description.

White, soft, fine filaments; insoluble in ordinary solvents; soluble in ammoniacal solution of copper oxide; ash, not more than 0.2 of 1 per cent. For details, see U.S.P., p. 183.

For *tests for identity*, for *impurities* (acid, alkali, fatty matter, dyes, water-soluble impurities), see U.S.P., p. 183.

Remarks.—This represents raw cotton freed from fat by boiling in a very dilute alkaline solution, and washing very thoroughly with water the first portion of which has been acidulated. It is commonly called *absorbent cotton.*

Raw cotton floats when placed in water, because each filament is coated with a layer of oil, rendering the cellulose impervious to water, which cannot, therefore, displace the air in the lumen (the cavity) of the cell. In this way each filament of raw cotton is buoyed up by the air within its lumen. Absorbent cotton is this raw cotton freed from its oily covering. Water is, therefore, able to penetrate the cellulose and thus displace the air in the lumen. The cellulose itself being heavier than water, the water-filled filaments sink; hence a pledget of absorbent cotton placed upon water immediately falls to the bottom of the vessel.

Purified cotton is used as a surgical dressing and as a filtering medium.

Linen, the fibers of stem of the flax consists of a modification of cellulose; *silk*, the fibers of the cocoon of the silkworm is a mixture of two protein substances—silk fibroin, silk gelatin; and *wool*, the hair of the sheep consists essentially of two proteins resembling keratin.

Paper originally represented a special form of shredded linen or cotton. The details of the manufacture of paper are beyond the scope of this book, but suffice it to say that the mass of shreds, when rolled out into paper, forms an absorbent sheet known as filter or blotting paper, according to its thickness. Writing paper represents this absorbent paper, which has been coated with a layer of some substance which ink will not penetrate, such as a combination of albumin, resin, or casein with aluminum salts. Most paper now used in printing is, however, made from wood fiber.

If cotton or linen paper is rapidly passed through 50 per cent sulfuric acid, the outer layer becomes converted into a starch modification (amyloid), forming the well-known product called *parchment paper.* If the paper is allowed to remain long in contact with sulfuric acid, it is converted into *dextrin,* which will dissolve in the acid. The same is true of absorbent cotton; it dissolves in concentrated sulfuric acid, but the solution in this case differs from the solution of the cotton in ammoniacal copper oxide, because in the acid it dissolves not as cellulose, but as dextrin, whereas the copper solution is a solution of the cellulose from which the cotton can be redeemed by simple methods.

Cotton or cellulose, like glucose and the sugars, is an alcohol, as is proved by the fact that when treated with a mixture of nitric acid and sulfuric acid it is converted into the ester, nitrocellulose. Several forms of nitrocellulose are known, these being grouped into two classes—the first, true pyroxylins, and the colloxylins.

The first, which is the true *gun cotton,* was discovered by Schoenbein in 1864, and has the formula $C_{12}H_{14}(ONO_2)_6O_4$, which, it will be noticed, contains six nitro groups.

The second series, the colloxylins, are respectively:

$$C_{12}H_{15}(ONO_2)_5O_5,$$
$$C_{12}H_{16}(ONO_2)_4O_6,$$
$$C_{12}H_{17}(ONO_2)_3O_7,$$

containing five, four, and three nitro groups. The true pyroxylin mentioned above is insoluble in a mixture of alcohol and ether, whereas the three colloxylins are soluble in a mixture of alcohol and ether. Which of these nitro bodies is produced depends on the proportion of nitric and sulfuric acids employed and the duration of maceration.

PYROXYLINUM—Pyroxylin

(Pyroxylin.—Soluble Gun Cotton)

Pyroxylin is a product obtained by the action of a mixture of nitric and sulfuric acids on cotton, and consists chiefly of cellulose tetranitrate, $C_{12}H_{16}O_6(NO_3)_4$.

Storage.—Preserve loosely packed in cartons, and protected from light and moisture.

Summarized Description.

Yellowish-white matted masses of filaments looking like raw cotton; harsh to touch; very inflammable; explosive; decomposes when kept in closed bottles; soluble in mixture of 3 volumes of ether and 1 volume of alcohol, also in acetone and in glacial acetic acid. For details, see U.S.P., p. 312.

For *tests for identity* and for *impurities* (soluble substances), see U.S.P., p. 312.

Remarks.—Pyroxylin consists of a mixture of the three colloxylins (chiefly the tetranitrate) given above, and is made, as mentioned above, by immersing cotton in a mixture of nitric acid and sulfuric acid. An interesting fact in the manufacture worth pointing out is that the macerating cotton should be carefully covered, as it has been noticed that if a mixture is allowed to stand in a dish, particles of dust and the like are apt to start a new reaction in the mixture, with the ultimate formation of dextrin and complete solution of the pyroxylin.

The manufacture of pyroxylin is simple, but the freeing of the cotton from acid is tedious, and usually takes a large quantity of water for the purpose. If pyroxylin is not freed from acid, it will assume a brown tint and decompose. The same decomposition occurs if pyroxylin is kept in well-stoppered bottles, hence the Pharmacopœia directs that it be kept in cartons.

The pyroxylin of the Pharmacopœia has an appearance similar to that of cotton, but possesses a harsh feel, rather than the softness of the pure cotton. It should be completely soluble in a mixture of 1 part alcohol and 3 parts ether, and this solution, containing 4 per cent of guncotton, is official under the name collodion (p. 233).

Guncotton is one of the most inflammable of substances, portions brought in contact with a flame instantly igniting with a brilliant light, and leaving no trace of ash behind. Its great inflammability makes it a rather dangerous product to have around, and, therefore, it should be handled with the utmost caution and kept remote from heat or fire. If guncotton be heated in a confined space, the same decomposition occurs with explosive violence, and it is, therefore, used as an explosive.

Its action, however, is too uncertain to make it safe for this purpose; hence nitroglycerin is preferred for blasting rather than guncotton.

A mixture of pyroxylin with camphor, whitened with zinc oxide, and made pliable with castor oil, forms the well-known commodity *celluloid*. This possesses the same inflammability as pyroxylin, and, therefore, its use in various articles of apparel, such as combs, is not to be recommended. Noninflammable formyl- and acetyl-cellulose products are now being made.

Rayon, or *artificial silk*, is prepared by treating cotton with certain chemicals producing cellulose products having the lustrous appearance of the product of the silkworm. In one process, the cotton is dissolved in an ammoniacal solution of copper oxide and is then precipitated by addition of acids. The pulp mass thrown down is "spun" by pressing through minute orifices. In another process, nitrocellulose is prepared and the nitric acid is then removed by treatment with alkali; while "viscose" silk is sodium-cellulose thiocarbonate, made by treating paper in strong alkali and macerating the mercerized cellulose thus obtained, with benzin and carbon disulfide. The thiocarbonate which results is then treated with 10 per cent alcoholic sulfuric acid and the resultant "viscose" is "spun" as described above. These substances can be "spun" in sheets and such "laminated silks" are now being sold under trade names as substitutes for sheet gutta-percha and oil silk as a protective coating for wounds.

Wood is cellulose which has become impregnated with *lignin*; as much as 30 per cent being present. Klason believes that lignin is a mixture of α-lignin, $C_{20}H_{20}O_6$ and β-lignin, $C_{19}H_{18}O_7$. The former is a condensation product of coniferyl aldehyde. Jonas differentiates between native lignin, $C_{22}H_{22}O_8$ and Willstatter lignin, $C_{20}H_{22}O_6$. The demand for cheap paper has led to the use of wood for the manufacture of paper instead of linen and cotton. Such paper is by no means so durable as that from pure cellulose, and it is often convenient to be able to decide whether a given sample of paper contains wood fiber. This is very beautifully determined by pouring on the suspected paper a solution of aniline acetate. If the paper is pure cellulose, no change of color will be produced, but with a slight amount of wood fiber the reagent will form a brilliant yellow. If paper is treated with a solution of phloroglucin, followed by a few drops of concentrated hydrochloric acid, a bright red stain results if wood fiber is present.

Cellophane is the name applied to cellulose films obtained by precipitating viscose solutions with ammonium chloride or ammonium sulfate. These films are elastic, stable to water, oil and alcohol, gas tight and noninflammable. The process of manufacture was patented in 1909 and in recent years it has become a very important article of commerce as wrapping material for foodstuffs.

Cellulose Lacquers.—These represent solutions of acetyl cellulose and similar cellulose compounds in organic solvents, such as mixtures of butyl and amyl alcohols, butyl, amyl and hexyl acetates and similar products. The types of cellulose materials employed are numerous and the number of solvent mixtures is very large; hence detailed description at this place is not possible, and the reader is referred to the bibliography found at the end of this chapter.

Starches represent bodies having the formula $(C_6H_{10}O_5)x$. As to its complex composition see pages 693 and 701.

Starch is formed in the leaves of plants from carbon dioxide and water under the influence of chlorophyl, as already explained on p. 650. It represents the great plant reserve stuff.

During the time it is in leaf the plant manufactures starch, which is then stored up as nourishment for the young shoots of the following spring. While starch is formed in the leaves of plants, as these leaves are shed by the plant in the winter it is necessary that starch be stored in some other organ during that period; hence the starch formed in the leaves is converted into sugar and is transported to the organs in which it will be reserved (very frequently the roots or rhizome), where it is changed back into starch. Likewise in the spring, the stored matter is converted once more into sugar, which passes in solution up to the growing part of the plant. This solution is known as "sap," and commercial advantage is taken of the sugar contents of sap in the preparation of *maple sugar*.

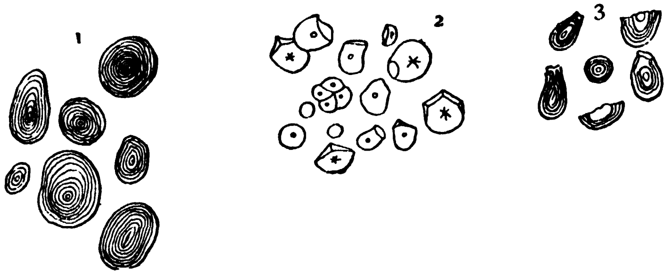


Fig. 269.—Microscopic appearance of different starches (uniform magnitude) (Noël): 1, arrowroot; 2, raw tapioca; 3, tapioca.

Starch is found in various parts of the plant, in particles called starch granules. The appearance of these granules is characteristic for the different varieties of starch, and some are shown in Fig. 269.

The concentric rings of typical starch granules are said to be due to two types of starch molecule; *alpha amylose* (water insoluble) and *beta amylose* (water soluble).

Hartwich and Wichmann have shown that a wheat starch granule weighs about 69 trillionths of a gram; while a potato starch granule weighs about 7.6 billionths of a gram.

The starches are usually insoluble in cold water, and on being treated with hot water swell into a paste, which is more or less soluble in water. The test for starch is that the addition of a drop of iodine to starch paste turns it blue.

As mentioned above, starch is converted by the enzyme diastase into maltose (p. 700), while the same starch treated with sulfuric acid is converted into glucose.

The most abundant starch is that from potato, from which it is extracted by a very simple process, grated potato being poured into troughs over which water is allowed to run, the water dissolving out the albuminates and other soluble principles, while the starch settles in the bottom of the trough in which it is collected. This potato starch is the well-known starch used in laundries, the starch for food or medicine being obtained either from corn or wheat.

AMYLUM—Starch

(Corn Starch)

Starch consists of the granules separated from the grain of *Zea mays* Linné (Fam. *Gramineæ*).

Starch contains but a trace of foreign organic matter and yields not more than 0.5 per cent of ash, and not more than 14 per cent of moisture (see U.S.P., p. 473).

Summarized Description.

Fine powder or irregular, annular, white masses, consisting of polygonal, spheroidal starch grains, insoluble in cold water and in alcohol; boiled with 15 parts of water it yields a jelly. For details, see U.S.P., p. 57.

For *tests for identity* and for *impurity* (iron), see U.S.P., p. 57.

Remarks.—The official starch is that from corn. As seen in the picture, starch granules from the same source are similarly marked, having more or less well-defined concentric rings radiating from a central spot called the hilum.

Arrowroot is a starchy product obtained from the rhizomes of *Maranta utilissima.* It is highly esteemed as a food for infants and invalids.

Starch Modifications.—*Lichenin* is a variety of starch found in Iceland moss. It does not turn iodine blue.

Inulin is a starch modification found in roots of the natural order *Compositæ.* It differs from starch in being soluble in water, from which it separates in crystalline form. It turns iodine yellow instead of blue.

Glycogen is a starch modification which is of interest only because of its animal origin, being found in the liver.

GUMMY SUBSTANCES

Gums have a composition similar to starch. They differ from starch in being either soluble in cold water or swelling to a jelly therein, and in being precipitated from aqueous solution by alcohol. On oxidation with nitric acid they yield mucic acid, while starch on treatment with nitric acid yields dextrin.

Among the gummy principles of pharmaceutic importance are the following:

Dextrin, made by oxidation of starch with nitric acid, this being the commercial method of manufacture.

It is also produced by simply heating starch, and it is of passing interest to note that the polish we see on the outer surface of a loaf of bread is due to the dextrinization of the starch of the flour, and to the same cause is due the high polish acquired by ironing well-starched linen.

Dextrin is a whitish-yellow body, dissolving in water to form mucilage, for which purpose it is chiefly employed. On account of the high price of gum arabic, dextrin has been suggested as an emulsifier for cod liver oil, and, in fact, a recipe for making an emulsion with dextrin was given in the third edition of the National Formulary. Such emulsions have never yielded satisfactory results in the writer's experience.

Arabic Acid.—This is the active principle of acacia, where it is found as the calcium salt (*arabin*). On hydrolysis it yields galacto-glucuronic acid, galactose, arabinose, and methyl pentose.

Bassorin is the chief constituent of gum tragacanth. It differs from dextrin in the fact that it does not dissolve in cold water, but simply swells to form mucilage.

Cerasin, or fruit gum, is the well-known exudation from peach and plum trees. It is insoluble in water, but dissolves in alkali.

Pectins are acid combinations of carbohydrates. They are found in various vegetable juices, and under the influence of an enzyme, *pectase,* they coagulate. This explains the manufacture of jellies from fruit juices, and also explains why preparations of some drugs, notably senega, gelatinize. Bertrand and Mallèvre found that calcium, or one of the other alkaline earths, is necessary to produce gelatinization, proving that the coagulated mass is the calcium salt of pectic acid, and not pectic acid itself.

The composition of pectin is still uncertain. McKinney states that ordinary pectin consists of four substances: (*a*) protopectin; (*b*) true pectin; (*c*) pectinic acid; (*d*) pectic acid. True pectin hydrolyzes to methanol and pectinic acid; pectinic acid, on boiling with hydrochloric acid, gives araban and pectic acid; pectic acid breaks down into galacturonic acid, galactose, and arabinose. In short, according to Ehrlich, true pectin consists of the calcium-magnesium salt of an anhydro-arabino-galactose-methoxy-tetragalacturonic acid.

Manna (U.S.P. X; N.F. VI) is the dried exudation of *Fraxinus Ornus.* It contains mannitol, sugar, dextrin and also *fraxin,* $C_{16}H_{18}O_{10}$. It exudes from the trunk of the manna ash during the heat of the day, solidifying in the chill evening air. The Formulary directs the use of what is commercially called "large-flake" or "small-flake" manna; "sorts" manna being rejected. A favorite method of administration is as "senna, manna, and salts" (*compound infusion of senna,* N.F., p. 238). It is used as a laxative. *Dose.*—15 Gm. (240 grains).

MEL—Honey

For *official definition,* see p. 225.

Summarized Description.

Thick, syrupy, light yellow or yellow-brown liquid; characteristic odor; sweet, faintly acrid taste; levorotatory; diluted with twice its weight of water, the liquid has sp. gr. of 1.099. For details, see U.S.P., p. 229.

For *tests for identity* and for *impurities* (starch, dextrin, foreign colors, azo dyes, invert sugar, chloride, sulfate), see U.S.P., p. 229.

Constituents.—Dextrose, levulose, traces of cane sugar, dextrin, and acetic, formic, malic, and citric acids, particles of wax. The color is due to carotin (p. 880).

Remarks.—Official honey represents the nectar extracted from flowers by the bee and stored in the honeycomb for food purposes.

That the bee is able to produce a chemical change in the nectar in transferring it from the flower to the comb is shown by the ability of captive bees to convert dextrogyrate sugar to levogyrate honey. *Mel* of U.S.P. XI is the *clarified honey* of U.S.P. IX, the latter name being a synonym in the present Pharmacopœia. For further details concerning honey and clarified honey, see p. 225.

Medical Properties.—Practically none, save as a pharmaceutic vehicle and as an excipient.

Prunum (U.S.P. VIII; N.F. V), or *Prune,* the partly dried ripe fruit of *Prunus domestica* Linné (Fam. *Rosaceæ*); contains sugar, malic acid, pectin, and is used as a laxative and nutritive. It is an ingredient of *confection of senna* (N.F. V).

Cassia Fistula (U.S.P. VIII; N.F. V), the dried fruit of *Cathartocarpus Fistula* Linné Persoon (Fam. *Leguminosæ*), contains sugar, gum, pectin, and citric acid and is an ingredient of *confection of senna* (N.F. V). It is a laxative in 60-grain doses.

Ficus (U.S.P. VIII; N.F. V), or *Fig,* is the partially dried fruit of *Ficus Carica* Linné (Fam. *Moraceæ*). It contains sugar, gum, nitrogenous bodies and small amounts of fruit acids. Figs are demulcent, laxative, and nutritive. It is a constituent of *confection of senna.*

Triticum (U.S.P. IX; N.F. VI), or *Dog Grass,* represents the dried rhizomes and roots of *Agropyron repens.* It contains levulose, triticin, malates and mucilage and is sometimes called *couch grass* and *quick grass*. It has already been discussed as yielding a fluidextract made with aqueous menstruum (p. 271). It is used as a diuretic in 10-Gm. doses.

Maltum (U.S.P. X), or *Malt*, is the grain of one or more varieties of *Hordeum vulgare* partially germinated artificially and containing amylolytic enzymes. Malt occurs in yellowish or amber-colored grains and it contains maltose and diastase. It was official as the material from which *extract of malt* (p. 301) was made.

MUCILAGINOUS DRUGS

A mucilaginous drug is one containing one of the gums, discussed from the chemical standpoint on p. 705. To what is there stated need only be added the warning that many substances commonly called "gums" are not true gums, in the modern pharmaceutic sense. Thus "gum elastic" (or rubber) and "chicle gum" (the basis of modern chewing gum) are dried milk juices; "gum asafetida" (p. 876) and "gum myrrh" (p. 877) are gum resins; "gum camphor" (p. 831) is the solid part of a volatile oil; "gum turpentine" (p. 862) is an oleoresin; "gum tolu" (p. 866) is a balsam; "gum mastic" (p. 873) and "gum benzoin" (p. 875) are resins, and so on.

What these substances—milk juices, gum resins, oleoresins, balsams, etc.—really are will be explained in the appropriate place, and here let it be said that a true gum is a carbohydrate derivative, more or less soluble in water (forming an adhesive solution or paste) and insoluble in alcohol.

ALTHÆA—Althea

(Marshmallow Root)

Althea is the dried root of *Althæa officinalis* Linné (Fam. *Malvaceæ*), deprived of the brown, corky layer and small roots.

Althea contains not more than 1 per cent of foreign matter.

Constituents.—Mucilage, asparagin (p. 684), starch, sugar, pectin.

Remarks.—This drug is commonly called "marshmallow root," and it might be said, in passing, that the confection, "marshmallow drops," originally contained this drug. Now it is innocent of such admixture, being made from sugar and gum dusted with cornstarch. Powdered althea is a valuable absorbent medium for making pills from liquids.

Medical Properties.—Demulcent, usually in the form of syrup (*syrupus althææ*, N.F., p. 223.

Sambucus (N.F. VI), or *Elder Flowers*, are obtained from *Sambucus canadensis* or *S. nigra*. They contain a small amount of volatile oil, mucilage and a yellow pigment, isolated by Lloyd and called by him, *eldrin*, which is identical with *rutin*, the pigment from eschscholtzia flowers.

Ulmus (U.S.P. X; N.F. VI), or *Slippery Elm*, is the dried inner bark of *Ulmus fulva*. It contains mucilage, trace of tannin and only a very little starch. It is used as a demulcent and emollient. The mucilage (*mucilago ulmi*, p. 215) is used as a basis of domestic cough remedies, while the ground bark is used as a soothing poultice. *Troches of Elm* (N.F. VI) is a popular remedy for bronchial coughs.

Sassafras Medulla (U.S.P. VIII; N.F. V), or *Sassafras Pith* is obtained from *Sassafras variifolium*. It contains a mucilage which is not precipitated from aqueous solution by alcohol. It is used as a demulcent and its cold infusion, *mucilago sassafras medullæ* (N.F. V) (p. 215), is used as a soothing basis for eye lotions.

AGAR—Agar

(Agar-Agar)

Agar is the dried mucilaginous substance extracted from *Gelidium corneum* (Hudson) Lamouroux and other species of *Gelidium* (Fam. *Gelidiaceæ*) and closely related algæ (Class *Rhodophyceæ*).

Agar contains not more than 1 per cent of foreign organic matter, and yields not more than 1 per cent of acid-insoluble ash, and not more than 18 per cent of moisture.

Constituents.—Chiefly gelose, a carbohydrate that hydrolyzes to galactose; ash (about 4 per cent) consisting largely of diatoms or fossilized microscopic plants.

Remarks.—Agar comes from the Orient and is prepared from sea weeds. It is now produced on a commercial scale in California. It occurs in thin, translucent membranes and boiled with 100 parts of water yields upon cooling a stiff jelly.

Medical Properties.—Now very popular as a mechanical remedy for constipation, by forming with the fluids of stomach and intestines a jelly which increases in bulk and causes a movement of the bowels. It is also used for making culture media in bacteriological work.

Dose.—10 Gm. (2½ drachms).

ACACIA—Acacia

(Acac.—Gum Arabic)

Acacia is the dried gummy exudation from the stems and branches of *Acacia Senegal* Wildenow, or of some other African species of *Acacia* (Fam. *Leguminosæ*).

Acacia yields not more than 1 per cent of water-insoluble residue, and not more than 4 per cent of total ash, not more than 0.5 per cent of acid-insoluble ash, and not more than 15 per cent of moisture.

Constituents.—Arabin, a levogyre gum, chiefly calcium salt of arabic acid. (See p. 705.) It also contains an oxydase that causes the color changes when it is mixed with guaiac.

Remarks.—Acacia is precipitated from solution by lead subacetate, ferric chloride, and saturated solution of borax; hence these substances should not be prescribed with mucilage of acacia; alcohol also precipitates the mucilage. A mucilage made from 3 parts of acacia and 6 parts of water will, however, stand the addition of 1 part of alcohol.

Medical Properties.—Demulcent. It is the most important pharmaceutic adhesive agent, and is employed for this purpose in emulsions. Official preparation: *mucilage of acacia* (p. 215).

TRAGACANTHA—Tragacanth

(Trag.—Gum Tragacanth)

Tragacanth is the dried gummy exudation from *Astragalus gummifer* Labillardière, or other Asiatic species of *Astragalus* (Fam. *Leguminosæ*).

Constituents.—Water-soluble gum, similar to arabin; bassorin, $(C_{11}H_{20}O_{10})x$ which does not dissolve in water, but simply swells therein, making a jelly; bassoric acid; cellulose.

Remarks.—Tragacanth differs from acacia in swelling to a jelly, when mixed with water, instead of dissolving therein, as does acacia. The official mucilage (*mucilago tragacanthæ*, p. 215) is largely used as a basis for jellies for chapped hands. It is also an excellent pill excipient. Powdered tragacanth is frequently adulterated with *Indian gum*, an exudation from *Sterculia urens* and with *sarcolla*, which is obtained from *Astragalus fasciculifolius*.

Medical Properties.—Demulcent.

Jujube is a paste prepared from the fruit of *Zizyphus jujube*. It contains from 62 to 75 per cent of sugars (see p. 352).

Quince Seed, obtained from *Cydonia vulgaris,* contains 22 per cent of mucilage in cells of the outer layer of the integuments. It yields on hydrolysis oxalic acid and arabinose. Renfrew and Cretcher also found compounds of aldobionic acid.

Plantaginis Semen (N.F. VI), or *Psyllium Seed,* is obtained from the familiar weed, the plantain. There are several species used in their home countries in folk medicine; notably *Plantago psyllium* (flea seed) cultivated in France and other parts of Europe and *Plantago ovata* (blond psyllium) grown in India. In its outer layer of cells, psyllium seed contains mucilage (about 10 per cent of the total weight of the seed) consisting of 9.85 per cent of pentosans and 0.31 per cent of galactans. Psyllium now enjoys enormous vogue as a mechanical intestinal lubricant; the whole seed being eaten mixed with a suitable cereal.

Dose.—8 Gm. (2 drachms).

Chondrus (N.F. VI), or *Irish Moss* or *Carragheen,* is the dried plant of *Chondrus crispus.* It contains pectin (*carragheenin*) mucus, pentose radicals, ethereal sulfates and traces of iodine and bromine. Much of the commercial product is bleached with sulfur dioxide. It is used as a demulcent and nutritive, being administered in the form of a jelly made by boiling 1 part of drug with 30 parts of water and letting strained solution cool. The decoction, carefully evaporated, and the syrupy residue poured on glass plates, yields scaled *Irish moss gelatin* (or *gelatinum chondri* N.F. IV), recommended by Emlen Painter as an emulsifying base. The *mucilage* is recognized by the National Formulary (p. 215).

Cetraria, the lichen *Cetraria islandica,* was official in former Pharmacopœias, but was dropped in the revision of 1890. It contains two mucilaginous principles, *lichenin,* $C_{12}H_{20}O_{10}$, and isolichenin, and a bitter principle, *cetraric acid,* now known to be a mixture. It also contains a small amount of fumaric acid. It was used as a nutritive in sick diet in the form of jelly (*decoctum cetrariæ,* U.S.P. 1890). For this purpose, however, the bitter cetraric acid had to be removed before jelly was made; hence the directions in making the decoction to throw away the first water in which the drug was washed.

BIBLIOGRAPHY

Mannitol.—(History) Proust (1806), through Beilstein, 1, 1893, 284. (Structure) Fischer, B., 23, 1890, 3684. (Manufacture) Genois, A.J.P., 53, 1881, 232; Scarlata, C.A., 15, 1921, 3365; Fenaroli, *ibid.*, 16, 1922, 2570.

Dulcit.—Bouchardat, A., 160, 1871, 338.

Sorbit.—Fischer, B., 23, 1890, 3684; Tanret, C.A., 25, 1931, 1552.

Carbohydrates.—(Structure) Fischer, B., 23, 1890, 2114; B., 24, 1891, 1836 and 2683 and B., 27, 1894, 3189; Tanret, Compt. rend., 120, 1895, 1060; Rosanoff, Jl. Am. Ch. Soc., 28, 1906, 114; Behrend and Roth, A., 331, 1904, 359; Haworth and co-workers, Jl. Ch. Soc., 113, 1918, 188; 115, 1919, 809; 123, 1923, 294; Armstrong and Hilditch, *ibid.*, 115, 1919, 1410; Picket, Jl. ph. ch., 23, 1921, 186; Hibbert and Hale, Jl. Am. Ch. Soc., 45, 1923, 736; Irvine, Jl. Ch. Soc., 123, 1923, 898; Zemplen, C.A., 21, 1927, 2121; Haworth, Jl. Soc. Ch. Ind., 45, 1926, 76; *ibid.*, 46, 1927, 527 and 295T; *ibid.*, 48, 1929, 240; Jl. Ch. Soc., 1927, 1040; Freudenberg and co-workers, C.A., 23, 1929, 108; Maltby, Jl. Ch. Soc., 1929, 2769; Cattelain, Jl. de ph. et ch., [8], 9, 1929, 70, 113 and 153; Hudson, Jl. Am. Ch. Soc., 52, 1930, 1707; Hibbert, Science, 73, 1931, 500; Armstrong, 50, 1931, 534; Eddy, Jl. Ch. Ed., 8, 1931, 1370; Sattler, *ibid.*, 8, 1931, 1369; Levene, Science, 73, 1931, 459; Ed., Jl. Soc. Chem. Ind., 51, 1932, 586.

Levulose.—(Commercial manufacture) Anon., Jl. Ind. Eng. Ch., 16, 1924, 1092; Jackson and co-workers, *ibid.*, 16, 1924, 1250; Dunton, C.A., 22, 1928, 3000; Collins and Gill, Jl. Soc. Ch. Ind., 45, 1926, 63T; McGlumphy and Eichinger, C.A., 26, 1932, 5355.

Calcium Gluconate.—Anon., Merck's Rep., 41, 1932, 53.

Mucic Acid.—Blicke and Powers, Jl. A.Ph.A., 16, 1927, 1146.

Glucose.—(History) Herstein, Jl. Ind. Eng. Ch., 3, 1911, 158. (Manufacture) Wiley, A.Ph.A., 30, 1882, 373; Rolfe, A.J.P., 87, 1915, 269; Newkirk, Jl. Ind. Eng. Ch., 16, 1924, 1173; Marks, Jl. Soc. Ch. Ind., 48, 1929, 224B. (Tests) Fehling, through Herstein, Jl. Am. Ch. Soc., 32, 1910, 779; Rosenkranz, C.A., 5, 1911, 2472; Fischer, B., 23, 1890, 2130; Rosenfield, Am. Dr., 18, 1889, 31; Fleury and Tavernier, 44, 1925, 418B.

Sugar.—(History) Geare, Merck's Rep., 24, 1915, 28; Martineau, Ch. News, 117, 1918, 359; Wiedemann, C.A., 15, 1921, 3220; Ed., Jl. Soc. Ch. Ind., 46, 1927, 1095; Armstrong, *ibid.*, 50, 1931, 756. (Synthesis) Pictet and Vogel, C.A., 22, 1928, 2743; 23, 1929, 376 and 4933; Gibson, Jl. Soc. Ch. Ind., 47, 1928, 355; Anon., Jl. Ind. Eng. Ch., News Ed., 6, May 10, 1928, 10; Irvine and co-workers, Jl. Soc. Ch. Ind., 47, 1928, 494. (Structure) Tollens, B., 16, 1883, 923; Fischer, B., 23, 1890, 2114; Ed., Jl. Soc. Ch. Ind., 44, 1925, 242. (Manufacture) Anon., Ph. Jl., 9, 1894, 220; Browne, A.J.P., 87, 1915, 10; Cross, C.A., 8, 1914, 2634; Poucher, Ph. Jl., 98, 1917, 467; Ralph, C.A.,

15, 1921, 4057; Pearson, Jl. Soc. Ch. Ind., 43, 1924, 246; Keyworth, Jl. Soc. Ch. Ind., 44, 1925, 723; Anon., *ibid.*, 45, 1926, 130; Kwantes, *ibid.*, 45, 1926, 282 and 638; Garrett, *ibid.*, 46, 1927, 1014; Adams, *ibid.*, 47, 1928, 366 and 179T; Fairrie, *ibid.*, 47, 1928, 97; Anon., *ibid.*, 48, 1929, 832; Ed., *ibid.*, 49, 1930, 49. (Properties) van Eck, C.A., 5, 1911, 2586; LaWall, A.J.P., 81, 1909, 394; Mondain-Monval, Jl. Soc. Ch. Ind., 44, 1925, 644B; Savinov, C.A., 23, 1929, 3825; Anon., Ph. Jl., 127, 1931, 218; Vavrinecz, C.A., 26, 1932, 1492.

Maple Sugar.—Thoreau, Early Spring in Massachusetts, 1881, 199; Snell, Jl. Soc. Ch. Ind., 44, 1925, 140T and 47, 1928, 498; Nelson, Jl. Am. Ch. Soc., 50, 1928, 2009; Sale and Wilson, Jl. Frank. Inst., 206, 1928, 271.

Caramel.—Adriani, Ch. News, 15, 1867, 252; Sherlock, Ch. News, 15, 1867, 282; Aulard, C.A., 7, 1913, 3677; Cunningham and Doree, Ph. Jl., 98, 1917, 408; Daniel, C.A., 13, 1919, 3035; Beal and co-workers, Jl. A.Ph.A., 12, 1923, 495 and 850.

Lactose.—(Structure) Fischer, B., 21, 1888, 2633; Haworth and Leitch, Jl. Ch. Soc., 113, 1918, 188. (General) Whittier, Chem. Rev., 2, 1925, 85. (Synthesis) Pictet and Vogel, Comp. rend., 185, 1927, 332; C.A., 23, 1929, 597. (Beta lactose) Hockett and Hudson, Jl. Am. Ch. Soc., 26, 1932, 426; Sharp, Jl. Soc. Ch. Ind., 51, 1932, 1101. (Manufacture) Kunz, Am. Dr., 13, 1884, 161; England, A.Ph.A., 50, 1902, 354; Pedersen, C.A., 7, 1913, 2632; Anon., Am. Dr., 66, 1918, 419.

Malt.—Moerck, A.Ph.A., 56, 1884, 305.

Maltose.—Moerck, see above; Haworth and Leitch, Jl. Ch. Soc., 115, 1919, 809; Hibbert and Hill, Jl. A.C.S., 45, 1923, 736; Hudson, *ibid.*, 46, 1924, 483; Ling, Jl. Soc. Ch. Ind., 46, 1927, 279T; Berlin, Jl. Am. Ch. Soc., 48, 1926, 1107.

Cellobiose.—Schorger, Jl. Soc. Ch. Ind., 49, 1930, 157T; Ed., *ibid.*, 51, 1932, 218.

Cellulose.—(Structure) Pfeiffer and Tollens, A., 210, 1881, 294; Green and Perkin, Jl. Ch. Soc., 89, 1906, 811; Bumcke and Wolffenstein, B., 32, 1899, 2493; Mosenthal, Jl. Soc. Ch. Ind., 30, 1911, 782; Hibbert, Jl. Ind. Eng. Ch., 13, 1921, 256 and 334; Jl. Am. Ch. Soc., 45, 1923, 735; Bergmann, C.A., 16, 1922, 2314; Karrer, Z. angew. Ch., 35, 1922, 85 and C.A., 16, 1922, 644; Von Euler, Ch. Zt., 45, 1921, 977 and 998; Irvine, C.A., 17, 1923, 1713 and Jl. Ch. Soc., 123, 1923, 518 and 898; Clément and Rivière, C.A., 18, 1924, 3714; Bary, *ibid.*, 18, 1924, 2074; Schorger, Jl. Ind. Eng. Ch., 16, 1924, 1274 and Jl. Soc. Ch. Ind., 49, 1930, 157T; Herzog, *ibid.*, 44, 1925, 440B; Pringsheim and co-workers, B., 58B, 1925, 2135; Gray, Jl. Ind. Eng. Ch., 18, 1926, 811; Haworth, Jl. Soc. Ch. Ind., 46, 1927, 527; Rigby, Jl. Am. Ch. Soc., 50, 1928, 3369; Hess and Trogus, C.A., 23, 1929, 5315; Oddo, C.A., 23, 1929, 699; Standinger and Schweitzer, B., 63B, 1930, 3132; Hauser, Jl. Ind. Eng. Ch., 21, 1929, 124; Clark, *ibid.*, 22, 1930, 474; Sheppard, *ibid.*, 23, 1931, 781; Freudenberg, Jl. Soc. Ch. Ind., 50, 1931, 287T; Haworth, C.A., 26, 1932, 2711 and 5921; Jl. Soc. Ch. Ind., 51, 1932, 218; Potter, *ibid.*, 51, 1932, 869. (Properties) Connerade, C.A., 9, 1915, 861; Hess, Messmer and Jagla, C.A., 17, 1923, 208; Neale, C.A., 20, 1926, 821.

Absorbent Cotton.—(History) Anon., Jl. Soc. Ch. Ind., 42, 1923, 266. (Manufacture) Anon., Ch. and Dr., 85, 1914, 453; Anon., Jl. A.Ph.A., 3, 1914, 1172; Roescheisen, Ph. Zt., 56, 1911, 67; Chaplet, C.A., 8, 1914, 2951; Gerrard, Ph. Jl., 96, 1916, 573. (Properties) Picon, Jl. de ph. et ch., [8], 1, 1925, 380.

Silk.—(Composition) Staedeler, A., 111, 1859, 12; Fischer and Skiba, Zt. physiol. Ch., 33, 1901, 177 and 35, 1902, 226; Abderhalden, C.A., 16, 1922, 3490; Utz, C.A., 17, 1923, 1333; Brossa, C.A., 20, 1926, 1997; Shelton and Johnson, Jl. Ind. Eng. Ch., 22, 1930, 387. (History) Ekert, Schw. Wsch. f. Ch. u. Ph., 51, 1913, 317.

Wool.—Trotman and co-workers, Jl. Soc. Ch. Ind., 45, 1926, 20T.

Parchment Paper.—Barlow, Ph. Jl., 16, 1857, 612; Anon., Ch. News, 9, 1868, 286.

Pyroxylin.—(History) Caldwell, A.J.P., 28, 1856, 4; Farwell, Merck's Rep., 23, 1914, 138. (Composition) Eder, A.Ph.A., 28, 1880, 296. (Manufacture) Saposhrukor, C.A., 1, 1907, 1324; Tedesco, C.A., 7, 1913, 891; MacDonald, C.A., 3, 1909, 1459.

Lacquers and Lacquer Solvents.—Garlick, Ind. Ch., 2, 1926, 437 and 499; Gabriel, Jl. Ind. Eng. Ch., 20, 1928, 1063; Ed., Jl. Soc. Ch. Ind., 47, 1928, 256; Hofmann and Reid, Jl. Ind. Eng. Ch., 21, 1929, 955; Park and Hopkins, *ibid.*, 22, 1930, 826; Johnson, Jl. Ind. Eng. Ch., 21, 1929, 688.

Celluloid.—Hyatt, Jl. Ind. Eng. Ch., 6, 1914, 158; Chandler, Jl. Ind. Eng. Ch., 6, 1914, 156; Worden, Ch. Eng., 17, 1913, 26.

Rayon.—Coblentz, Pract. Dr., 28, 1910, 72; Semenov, C.A., 6, 1912, 1525; Bonwitt, Zt. angew. Ch., 26, 1913, 89; Verda, Schw. Wsch. f. Ch. u. Ph., 50, 1912, 301; Wilson, Jl. Soc. Ch. Ind., 36, 1917, 817; Snell, *ibid.*, 45, 1926, 925; Heuser and Schuster, *ibid.*, 45, 1926, 399B; Blanco, Jl. Ind. Eng. Ch., 18, 1926, 1257; Anon., Jl. Soc. Ch. Ind., 47, 1928, 372.

Cellophane.—Fox and Hall, Jl. Soc. Ch. Ind., 46, 1927, 282T; Anon., *ibid.*, 47, 1928, 598.

Lignin.—Klason, C.A., 4, 1910, 1805; 14, 1920, 2167; 15, 1921, 526 and 859; 16, 1922, 2487; B., 56B, 1923, 302 and C.A., 26, 1932, 6132; Hägglung, 14, 1922, 943; Crocker, Jl. Ind. Eng. Ch., 13, 1921, 625; Powell and Whittaker, Jl. Soc. Ch. Ind., 44, 1925, 201B; Hoffmeister, C.A., 22, 1928, 399; Jonas, C.A., 22, 1928, 3395; Freudenberg and Braun, C.A., 22, 1928, 3635; Fuchs and co-workers, C.A., 24, 1930, 236 and 26, 1932, 470; Herzog and Hillmer, C.A., 25, 1931, 4277; Holmberg, C.A., 25, 1931, 4309; Phillips, Science, 73, 1931, 568; Pavolini, C.A., 26, 1932, 2173; Hawley and Harris, Jl. Ind. Eng. Ch., 24, 1932, 873.

Paper.—Keenan, Ch. Eng., 18, 1913, 148 and Am. Dr., 67, 1919, 339; Huebner, Jl. Soc. Ch. Ind., 42, 1923, 227; Schwalbe, Jl. Soc. Ch. Ind., 48, 1929, 49B; Strachan, C.A., 24, 1930, 722; Roschier, Jl. Soc. Ch. Ind., 49, 1930, 278B; Kanamaru, C.A., 25, 1931, 4704.

Starch.—(Origin) Clark, Proc. 8th Int. Cong. App. Ch., 19, 1912, 55. (Composition and structure) Kraemer, A.J.P., 79, 1907, 217 and 412; Ling, Jl. Soc. Ch. Ind., 28, 1909, 31; Jl. Soc. Ch. Ind., 46, 1927, 279T; *ibid.*, 48, 1929, 291; Fouard, Comp. rend., 146, 1909, 978; Gruzewska, C.A., 7, 1913, 89; Hartwich and Wichmann, Arch. d. Pharm., 250, 1912, 452; Karrer, C.A., 16, 1922, 1745, 1746 and 2314; Irvine, Jl. Ch. Soc., 123, 1923, 898; Pringsheim and Steingroever, C.A., 19, 1925, 974; Pictet, C.A., 20, 1926, 1342 and Jl. Soc. Ch. Ind., 48, 1929, 695B; Alsberg, Jl. Ind. Eng. Ch., 18, 1926, 190; Taylor and Lehrmann, Jl. Am. Ch. Soc., 48, 1926, 1739; Nanji and Beazeley, Jl. Soc. Ch. Ind., 45, 1926, 215T; Tweedy, *ibid.*, 46, 1927, 682; Taylor and Beckmann, Jl. Am. Ch. Soc., 51, 1929, 274; Carr, Science, 69, 1929, 407; Effront, Comp. rend., 190, 1930, 1170; Morozov, C.A., 26, 1932, 5078; Caesar, Jl. Ind. Eng. Ch., 24, 1932, 1433; Morris, also Keresztesy, Inaugural Dissertations, Columbia Univ., 1934. (Manufacture) Anon., Dr. Circ., 57, 1913, 686. (Properties) Brown and Heron, A., 199, 179, 165. (Tests) Staiger, C.A., 22, 1928, 2706; Turner, C.A., 24, 1930, 4234.

Cerasin.—Kutzing, Arch. d. Pharm., 117, 1851, 9; Petry, C.A., 26, 1932, 1640; Butler and Cretcher, Jl. Am. Ch. Soc., 53, 1931, 4160.

Lichenin.—Tanret, Jl. de ph. et ch., 27, 1893, 449; Asano and co-workers, C.A., 25, 1931, 4266 and 26, 1932, 5067.

Arrowroot.—Wright, Trop. Agricult., 5, 1928, 162.

Glycogen.—Bernard, A.Ph.A., 21, 1873, 252; Pringsheim and co-workers, C.A., 24, 1930, 3996; Daoud and Ling, Jl. Soc. Ch. Ind., 50, 1931, 365T; Harmsen, C.A., 26, 1932, 5317.

Inulin.—Pringsheim and co-workers, C.A., 15, 1921, 3463; 16, 1922, 3878; 23, 1929, 377 and 24, 1930, 3996; Irvine, Jl. Ch. Soc., 123, 1923, 895; Karrer, C.A., 16, 1922, 1745; Haworth and co-workers, C.A., 22, 1928, 1959 and 26, 1932, 4799; Yanovsky and Kingsbury, Jl. Am. Ch. Soc., 53, 1931, 1597.

Dextrin.—(History) Simmonds, A.J.P., 29, 1857, 74; Dougal, Jl. Soc. Ch. Ind., 49, 1930, 595. (Manufacture) Procter, A.J.P., 11, 1840, 265; Petit, Ph. Jl., 51, 1892, 831. (Properties) Babington, Tingle and Watson, A.J.P., 91, 1919, 50; Biltz and Truthe, C.A., 7, 1913, 2572.

Arabic Acid.—Anon., A.J.P., 32, 1860, 366; Guérin, A.J.P., 4, 1832, 158.

Bassorin.—Guérin, A.J.P., 4, 1832, 158; O'Sullivan, Jl. Ch. Soc., 79, 1901, 1177; Maiden, Ph. Jl., 50, 1890, 7.

Pectin.—Braconnet, Jl. de Ph., 26, 1840, 372; Bertrand and Mallèvre, Comp. rend., 121, 1895, 726; Tschirch and Rosenberg, A.Ph.A., 56, 1908, 366; Frier, Jl. ph. ch., 16, 1917, 339; Ehrlich, Ch. Ztg., 41, 1917, 197; Gaertner, C.A., 14, 1920, 1455; Tutin, C.A., 17, 1923, 2291; Sucharipa, Jl. Am. Ch. Soc., 46, 1924, 145; Charpentier, C.A., 18, 1924, 3204; Dore, Jl. Ind. Eng. Ch., 16, 1924, 1042; C.A., 20, 1926, 2376; C.A., 21, 1927, 2155; Smolenski, C.A., 19, 1925, 41; and 22, 1928, 4109; Wilson, Jl. Ind. Eng. Ch., 17, 1925, 1065; Ehrlich, Jl. Soc. Ch. Ind., 44, 1925, 254B; C.A., 23, 1929, 5465; 25, 1931, 1989; 26, 1932, 5110 and 5586; Paton, Jl. Soc. Ch. Ind., 44, 1925, 1141; Norris, C.A., 21, 1927, 758; Mehlitz, C.A., 20, 1926, 3753; McKinney, Jl. Soc. Ch. Ind., 45, 1926, 301T; Savoja, C.A., 24, 1930, 171; Romeo, C.A., 24, 1930, 5080; Bottini, C.A., 24, 1930, 5389; Ziegelmayer, C.A., 24, 1930, 5389; Leone, C.A., 25, 1931, 362; Bridel, Jl. de ph. et ch., [8], 13, 1931, 99; Wegener, Ch. Zt., 55, 1931, 473.

Manna.—(History) Hanbury, A.J.P., 42, 1870, 162. (Source) Holmes, Ch. and Dr., 92, 1920, 25. (Constituents) Buignet, Jl. Ph. et Ch., 8, 1868, 5; Flückiger, Pharmacographia, 1874, 370. (Properties) LaWall and Forman, Jl. A.Ph.A., 6, 1917, 22.

Honey.—(Formation) Maeterlinck, Life of the Bee; Korndoerfer, Ap. Zt., 26, 1911, 659; Giersberger, C.A., 5, 1911, 538; Park, C.A., 23, 1929, 635; Farrar, C.A., 25, 1931, 4629. (Constituents) Muttelet, C.A., 5, 1911, 1131; Heiduschka, Schw. Wsch. f. Ch. u. Ph., 49, 1911, 725; Schuette and Bott, Jl. Am. Ch. Soc., 50, 1928, 1998; Nelson, Jl. Ind. Eng. Ch., 22, 1930, 448; *ibid.*, 23, 1931, 335; Gillette, C.A., 25, 1931, 4289; Lothrop and Paine, Jl. Ind. Eng. Ch., 23, 1931, 71. (Properties) Lampitt and co-workers, C.A., 25, 1931, 362; Dyce, 25, 1921, 4323.

Prune.—(Constituents) Koenig, Nahrungsmittel, 2, 1880, 397.

Cassia Fistula.—(Constituents) Griebel, C.A., 5, 1911, 1948.

Figs.—Paladino, A.Ph.A., 58, 1910, 221; Nelson, Jl. Am. Ch. Soc., 50, 1928, 2012.

Triticum.—Mueller, Arch. d. Pharm., 202, 1873, 500 and 203, 1873, 1; Hommell, Pract. Dr., 44, Nov., 1926, 25.

Althea.—(Constituents) Boutron-Charlard and Pelouze, Jl. de Ph., 19, 1833, 208; Schirmer, Arch. d. Pharm., 250, 1912, 230; Von Friedrichs, Ph. Week., 56, 1919, 1571; Will, C.A., 25, 1931, 3433; Dubsky, *ibid.*, 26, 1932, 4413.

Agar.—(Sources) Hamburg, [2], 1, 1860, 508; Marchand, A.J.P., 52, 1880, 573; (Constituents) Payen, Ch. News, 1, 1860, 34 and 35. (Properties) Fairbrother and Mastin, Jl. Soc. Ch. Ind., 42, 1923, 844A; Phillips, Pharm. Era, 62, June 5, 1926, 17; Anon., Pract. Dr., Dec., 1926, 36; Robertson, Jl. Ind. Eng. Ch., 22, 1930, 1074. (Medical Properties) Anon., Pacific Pharm., 5, 1911, 66.

Elm.—(Constituents) Johansen, Arch. d. Pharm., 209, 1876, 210; Schirmer, see above.

Sassafras Pith.—(Constituents) Schirmer, see above.

Acacia.—(Origin) Edie, Rep. Wellcome Trop. Research, Lab., 4, 1911, 73. (Constituents) Graeger, Ph. Jl., [3], 3, 1873, 973; Kiliani, B., 20, 1887, 339; Schaer, Schw. Wsch. f. Ch. u. Ph., 50, 1912, 325; Fowler and Malandkar, C.A., 20, 1926, 60; Weinman, C.A., 23, 1929, 5468; Butler and Cretcher, Jl. Am. Ch. Soc., 51, 1929, 1519; Giral, Jl. Soc. Ch. Ind., 49, 1930, 211B; Norman, C.A., 23, 1929, 4842; Heidelberger and Kendall, C.A., 24, 1930, 1625; Pfau, Apoth. Zt., 26, 1932, 1466. (Properties) "Dr. B.," Ph. Zt., 55, 1910, 232; Waters and Tuttle, Jl. Ind. Eng. Ch., 8, 1916, 413; Ridgway, C.A., 15, 1921, 773; Amy, C.A., 23, 1929, 478; Thomas and Murray, C.A., 22, 1928, 2503; Rosenthaler, Ph. Zt., 74, 1929, 317; Tschirch and Flück, C.A., 23, 1929, 5010; Gabel, Jl. A.Ph.A., 19, 1930, 828; Taft and Malm, C.A., 25, 1931, 3219 and 26, 1932, 5245; Laursen, C.A., 26, 1932, 3873. (Tests) Waters and Tuttle, C.A., 10, 1916, 1147; Weinberger and Jacobs, Jl. A.Ph.A., 18, 1929, 34; Jacobs and Jaffe, Jl. Ind. Eng. Ch., 23, 1931, 210. (Medical Uses) Schwartze and co-workers, 24, 1930, 5381.

Tragacanth.—(Sources and collection) Anon., Yearbook, A.Ph.A., 9, 1920, 338; Peyer, Ph. Zent., 65, 1924, 637. (Constituents) Guibourt, A.J.P., 6, 1834, 42; O'Sullivan, Jl. Ch. Soc., 79, 1901, 1164; Von Fellenberg, C.A., 9, 1915, 624; Sullivan, Ph. Cent., 62, 1921, 582; Evers and McLachlin, Ph. Jl., 113, 1924, 94 and 132; Norman, Biochem. Jl., 25, 1931, 200. (Adulterants) Feil, A.Ph.A., 57, 1909, 218; Fromme, C.A., 6, 1912, 3311; Scoville, Dr. Circ., 53, 1909, 116; Hooper, C.A., 8, 1914, 989; Tschirch and Flück, C.A., 23, 1929, 5010. (Tests) Gabel, Jl. A.Ph.A., 17, 1928, 1206; Konnerth, *ibid.*, 18, 1929, 698; Fischer, *ibid.*, 18, 1929, 889.

Chondrus.—(Constituents) Herberger, Rep. f. d. Ph., 49, 1834, 184. Painter, A.Ph.A., 35, 1887, 578; Haas, Ch. and Dr., 94, 1921, 75. (Adulteration) LaWall and Harrisson, Jl. A.Ph.A., 21, 1932, 1146. (Test) Ewe, Jl. A.Ph.A., 19, 1930, 568.

Cetraria.—(Constituents) Feuchtwanger, A.J.P., 6, 1834, 204; Herberger, Jl. de Ph., 23, 1837, 505; Berg, Jl. de Ph. et Ch., 18, 1873, 154; Hilger and Buchner, B., 23, 1890, 461; Haas, C.A., 15, 1921, 3865; Russell-Wells, Jl. Soc. Ch. Ind., 41, 1922, 996A; Salkowski, Jl. ph. ch., 23, 1921, 392; Karrer and Joos, C.A., 17, 1923, 3323; *ibid.*, 19, 1925, 1853; von Lingelsheim, C.A., 22, 1928, 2809; Kofler and Ratz, Arch. d. Pharm., 270, 1932, 338. (Properties) Haas, Ph. Jl., 106, 1921, 485.

Jujube Paste.—Church, C.A., 18, 1924, 2048.

Quince Seed.—Renfrew and Cretcher, Jl. Frank. Inst., 214, 1932, 510; Dickhart, A.J P., 104, 1932, 335.

Psyllium Seed.—Hepburn and Laughlin, A.J.P., 102, 1930, 565; Anon., Ph. Era, 67, 1930, 349; Anon., Pract. Dr., 49, Sept., 1931, 24; Figg, Ph. Jl., 126, 1931, 29; Christensen, Dr. Circ., 76, Apr., 1932, 14.

CHAPTER XL

GLUCOSIDES AND GLUCOSIDAL DRUGS

THE large and important class of plant principles called glucosides are ethers of glucose with complex bodies, the usual definition of glucosides being *bodies which, when treated with a diluted acid or a ferment, split into glucose and other substances.*

These "other substances" are usually of complex character. In most cases they are compounds of benzene, and as the knowledge of these derivatives is extended and they are placed in their proper position in systematic chemistry, the glucoside in question can be more properly studied under such heading. Thus we are confronted with this condition in the glucosidal drugs bitter almond and black mustard. In each case the product of hydrolysis is of more pharmaceutic importance than is the glucoside itself, hence black mustard is studied among the thiocyanates (p. 753), while the bitter almond is considered along with benzaldehyde (p. 793).

Even the word "glucose," used in the above definition, does not indicate the definite chemical we know by that name. As already learned, there are a large number of bodies having the formula $C_6H_{12}O_6$, and "glucose" in the above definition means any one of these. More than that, some glucosides yield bioses (for example Haworth and Leitch believe amygdalin contains maltose) while others yield carbohydrates other than hexoses; thus, digitalin is said to yield digitalose, $C_7H_{14}O_5$.

Rosenthaler has attempted a classification of glucosides which we condense in the following table. In this, the word "aglycone" refers to the "other substances" produced by the hydrolysis of the glucosides.

A. *Glucosides with nitrogen-free aglycones.*
- I. Yielding *aliphatic aglycones.*
  - (*a*) *Alcohols.* }
  - (*b*) *Aldehydes.* } Of little importance.
  - (*c*) *Ketones.* }
  - (*d*) *Acids.* Examples, jalapin, convolvulin and glycyrrhizinic acid.
- II. *α*. Yielding *aromatic aglycones.*
  - *Benzene derivatives.*
    - (*a*) *Alcohols.* Of little importance.
    - (*b*) *Phenols.* Examples, arbutin and methyl-arbutin.
    - (*c*) *Phenolic alcohols.* Examples, salicin and populin.
    - (*d*) *Phenolic acids.* Examples, gallic acid and tannic acid glucosides.
  - *β*. Yielding *styrol derivatives.*
    - (*a*) *Alcohols.* Examples, coniferin and syringin.
    - (*b*) *Phenolic acids and lactones.* Examples, caffetannic acid, daphnin, æsculin and fraxin.
    - (*c*) *Phenolic esters.* Example, hesperidin.
  - *γ*. *Anthracene derivatives.* Examples, frangulin and barbaloin.
- III. Yielding *heterocyclic aglycones.*
  - *a*. *Flavone derivatives.* Examples, quercetin.

B. *Glucosides with aglycones containing nitrogen.*
- I. Yielding *aliphatic aglycones.* Of little importance.
- II. Yielding *aromatic aglycones.* Example, amygdalin and similar glucosides.

C. *Glucosides with aglycones containing nitrogen and sulfur.*
- I. Yielding *aliphatic aglycones.* Example, sinigrin.
- II. Yielding *aromatic aglycones.* Example, sinalbin.

The word "*hydrolysis*" used above expresses the process of decomposing chemical substances by introducing the elements of water, this being the function of the diluted acid or the ferment in the decomposition of glucosides, as expressed in the following equations, illustrative of a few examples of such decomposition of glucosides:

Amygdalin plus Water equal Glucose plus Hydrocyanic acid plus Benzaldehyde.

$$C_{20}H_{27}NO_{11} + 2H_2O = 2C_6H_{12}O_6 + HCN + C_6H_5CHO$$

Arbutin plus Water equals Hydroquinone plus Glucose.

$$C_{12}H_{16}O_7 + H_2O = C_6H_6O_2 + C_6H_{12}O_6$$

Convallarin equals Glucose plus Convallaretin.

$$C_{25}H_{40}O_{10} = C_6H_{12}O_6 + C_{19}H_{28}O_4$$

Digitalin equals Digitaligenin plus Glucose plus Digitalose.

$$C_{35}H_{56}O_{14} = C_{22}H_{30}O_3 + C_6H_{12}O_6 + C_7H_{14}O_5$$

Digitoxin plus Water equals Digitoxigenin plus Digitoxose
$C_{41}H_{64}O_{13} + 3H_2O = C_{23}H_{34}O_4 + 3C_6H_{12}O_4$

Digitonin plus Water equals Digitogenin plus Glucose plus Arabinose
$C_{55}H_{90}O_{29} + 5H_2O = C_{26}H_{42}O_5 + 4C_6H_{12}O_6 + C_5H_{10}O_5$

Gentiopicrin plus Water equal Gentiogenin plus Glucose.
$C_{16}H_{20}O_9 + H_2O = C_{10}H_{10}O_4 + C_6H_{12}O_6$

Glycyrrhizin plus Water equal Glycyrrhetinic Acid plus Glycuronic Acid.
$C_{44}H_{64}O_{19} + 2H_2O = C_{32}H_{48}O_7 + 2C_6H_{10}O_7$

Ipuranol plus Water equal Dextrose plus Phytosterol.
$C_{33}H_{56}O_6 + H_2O = C_6H_{12}O_6 + C_{27}H_{46}O$

Myronic Acid plus Water give Glucose plus Potassium Bisulfate plus Oil Mustard.
$C_{10}H_{16}KO_9NS_2 + H_2O = C_6H_{12}O_6 + KHSO_4 + C_3H_5CSN$

Parillin plus Water equal Parigenin plus Glucose plus Rhamnose.
$C_{44}H_{72}O_{17} + 3H_2O = C_{26}H_{42}O_3 + 2C_6H_{12}O_6 + C_6H_{12}O_5$

Salicin plus Water equal Glucose plus Saligenin.
$C_{13}H_{18}O_7 + H_2O = C_6H_{12}O_6 + C_7H_8O_2$

Solanin plus Water equal Solanidin plus Dextrose plus Galactose plus Rhamnose.
$C_{52}H_{91}O_{18}N + H_2O = C_{34}H_{57}O_2N + C_6H_{12}O_6 + C_6H_{12}O_6 + C_6H_{12}O_5$

The following glucosides have been studied, but not sufficiently to furnish complete equation:

Chiratin hydrolyzes to ophelic acid and chiratogenin.
Colocynthin hydrolyzes to colocynthein and sugar.
Convallamarin hydrolyzes to convallamaretin.
Ericolin hydrolyzes to ericinol.
Hesperidin hydrolyzes to rhamnose, glucose, and hesperetin.
Scammonin hydrolyzes to scammonol, valerianic acid, and grape sugar.
Saponin hydrolyzes to glucose and sapogenin.
Strophanthin hydrolyzes to glucose, cymarose, and strophanthidin.

SAPONINS

Under the head saponin we include a large number of glucosides frothing like soap when shaken with water, usually toxic and, while similar, are not identical in chemical composition, nor is the hydrolysis product, sapogenin, identical in each case.

In 1911, Kobert described 44 saponins and classified them into two groups: those having the general formula, $C_nH_{2n-8}O_{10}$ and those of the formula $C_nH_{2n-16}O_{28}$. Investigations since that time have indicated a far greater complexity than the above formulæ indicate, so at this place a tabulation of the more important saponins is in order. The following are of pharmaceutic interest:

Senegin hydrolyzes to Seneginin.
$(C_{18}H_{28}O_{10})x \qquad C_{26}H_{44}O_6$

Quillajic Acid hydrolyzes to Sapogenin.
$(C_{19}H_{30}O_{10})_3 \qquad C_{29}H_{46}O_5$

Sarsa-saponin hydrolyzes to Sapogenin.
$(C_{22}H_{36}O_{10})_{12} \qquad (C_{14}H_{22}O_3)_2$

Parillin hydrolyzes to Parigenin.
$C_{44}H_{72}O_{17} \qquad C_{26}H_{42}O_3$

Digitonin hydrolyzes to Digitogenin (see above).
$C_{55}H_{90}O_{29}$

Guaiac Saponin hydrolyzes to Guagenin.
$C_{30}H_{48}O_3$

Gitonin hydrolyzes to Gitogenin.
$C_{49}H_{80}O_{23} \qquad C_{26}H_{42}O_4$

Van der Haar and other investigators have shown that some sapogenins are terpene derivatives, some are naphthalene derivatives, while others yield products resembling cholesterol.

GLUCOSIDAL SYNTHESES

The hydrolysis of glucosides outlined on page 713 pointed out the possibility of synthesizing the aglycon and the carbohydrates into the glucoside itself. By the purely chemical reaction between hydroquinone and acetobromoglucose Mannich synthesized arbutin. More interesting, however, are the biochemical syntheses conducted by Bourquelot and his coworkers. Starting with the aglycon and the carbohydrate under influence of certain enzymes, such as emulsin and yeast ferments, these investigators have prepared a large number of simple artificial glucosides, such as combinations of methyl alcohol and glucose. Similar work has been done by Emil Fischer and his pupils while the synthesis of the natural glucoside, amygdalin, was accomplished by Haworth and Campbell in 1924.

GLUCOSIDAL DRUGS

As mentioned above, glucosides owe their characteristics primarily to those products of hydrolysis other than glucose, and as these products possess widely varying properties, the grouping of glucosidal drugs brings together agents showing marked difference in medical action. In an attempt to bring a semblance of order into this therapeutic confusion the drugs considered in this chapter will be grouped as follows:

Drugs containing sweet glucosides	Glycyrrhiza.
Drugs containing bitter glucosides	Gentian.
Drugs containing glucosides acting on heart	Strophanthus, squill, and digitalis.
Drugs containing purgative glucosides	Lappa, jalap, ipomœa, scammony root, colocynth pulp.
Drugs containing astringent glucosides	Uva ursi.
Drugs containing saponin	Sarsaparilla and senega.

GLYCYRRHIZA—Glycyrrhiza

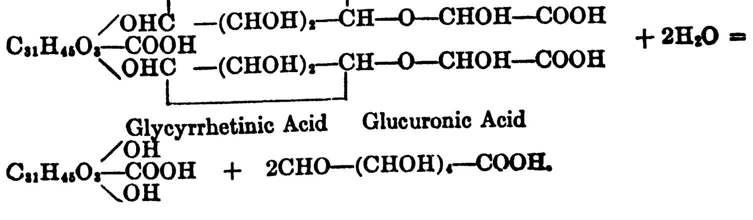
(Glycyrrh.—Licorice Root)

Glycyrrhiza is the dried rhizome and roots of *Glycyrrhiza glabra* Linné var. *typica* Regel et Herder, known in commerce as Spanish Licorice, or of *Glycyrrhiza glabra* Linné var. *glandulifera* Waldstein et Kitaibel, known in commerce as Russian Licorice, or of other varieties of *Glycyrrhiza glabra* Linné yielding a yellow and sweet wood (Fam. *Leguminosæ*).

Glycyrrhiza yields not more than 2.5 per cent of acid-insoluble ash.

Constituents.—*Glycyrrhizin or glycyrrhizic acid,* the potassium and calcium salts being the combination found in the drug; glucose, sucrose, mannitol, asparagin, fat and resin, glycyrrhamarin; and a trace of volatile oil.

Tschirch's researches show that glycyrrhizin is not a true glucoside since its hydrolysis product is not an ordinary carbohydrate. The following gives both the hydrolysis equation and the graphic formulæ of the ingredients and reaction products.



$$\mathrm{C_{31}H_{45}O_3}\begin{cases}\mathrm{OHC-(CHOH)_2-CH-O-CHOH-COOH}\\ \mathrm{COOH}\\ \mathrm{OHC-(CHOH)_2-CH-O-CHOH-COOH}\end{cases} + \mathrm{2H_2O} =$$

$$\mathrm{C_{31}H_{45}O_3}\begin{cases}\mathrm{OH}\\ \mathrm{COOH}\\ \mathrm{OH}\end{cases} + \mathrm{2CHO-(CHOH)_4-COOH}.$$

Galassi believes that glycyrrhizin is an ether of gluconic acid, rather than a glucuronic compound.

Remarks.—The Pharmacopœia permits the use of both Spanish and Russian licorice, the latter being larger than the Spanish, and comes into commerce peeled. It is sweeter than the Spanish, hence preferable.

Medical Properties.—Demulcent and expectorant. Used largely to disguise the taste of quinine and other bitter substances, for which purpose *ammoniated glycyrrhizin* (U.S.P. IX) or the *fluidextract* (p. 269) is used.

The other official preparations of glycyrrhiza are the *elixir* (p. 227), *pure extract* (p. 301), *brown mixture* (p. 279), and *compound licorice powder* (p. 316) now known as compound powder of senna.

Dose.—2 Gm. (30 grains).

Glycyrrhizinum Ammoniatum (U.S.P. IX), or *Ammoniated Glycyrrhizin*, occurs in dark brown or reddish-brown, water-soluble scales, having a very sweet taste. It represents glycyrrhizin in more or less impure form, is made by precipitation from an ammoniacal aqueous percolate of glycyrrhiza by means of sulfuric acid. The crude precipitated glycyrrhizin is dissolved in ammonia water and water, is reprecipitated with acid, again dissolved in ammonia water and water, and then "scaled" (p. 574).

Dose.—250 mg. (4 grains). This product is used entirely for masking taste of bitter substances.

GENTIANA—Gentian

(Gentian.—Gentian Root)

Gentian is the dried rhizome and roots of *Gentiana lutea* Linné (Fam. *Gentianaceæ*).

Gentian yields not less than 30 per cent of water-soluble extractive, and contains not more than 10 per cent of moisture, and not more than 2 per cent of foreign organic matter.

Constituents.—*Gentiopicrin,* a bitter glucoside; *gentianin,* a bitter principle; *gentisin,* when fused with potassa, yields *gentisic acid* (dihydroxybenzene-carboxylic acid) a body that turns deep blue with ferric chloride; *gentianose,* $C_{18}H_{32}O_{16}$, a crystalline sugar hydrolyzing to gentiobiose and levulose; etc.

Gentiobiose is a disaccharide resembling isomaltose. Both were synthesized by Pictet in 1925.

Gentian contains no tannin, the darkening of its preparations by iron salts being due to gentisin and gentisic acid.

Remarks.—The composition of the drug depends largely upon the method of drying. (See p. 127.) The usual method of air drying involves a certain degree of fermentation and such a product contains less gentiopicrin than a sample dried quickly in heated air.

Gentian preparations yield unsightly mixtures when combined with iron unless the gentisin is removed by treatment of the preparation with ferric hydroxide or unless tincture of citrochloride of iron, N.F., is employed.

The National Formulary gives recipes for three elixirs of gentian. (See p. 229.) Of these, the most popular is the *glycerinated elixir of gentian* which is similar to the so-called "glycerin tonic," which is largely prescribed.

Medical Properties.—Simple bitter; stimulates digestion and improves the appetite.

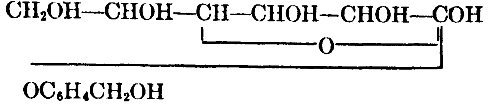
Administered as *fluidextract* N.F. V (p. 271) and as *compound tincture of gentian* U.S.P. X (p. 248). The *extract,* N.F. VI (p. 303), is a useful excipient for tonic pills, but should not be used for this purpose by a pharmacist unless so prescribed by the physician.

Dose.—1 Gm. (15 grains).

Chirata (U.S.P. VIII; N.F. V) is the dried plant of *Swertia Chirayita* (Roxburgh) Hamilton (Fam. *Gentianaceæ*). It contains *ophelic acid* and *chiratin*, the latter a glucoside. It is an East Indian herb of intensely bitter taste, little used in this country, but quite popular in England, and is used as a simple bitter in 15-grain doses.

Salicinum (U.S.P. X; N.F. VI), or *Salicin*, is a glucoside obtained from several species of *Salix* and *Populus*. It is prepared by making an aqueous infusion of willow bark, precipitating the gum and starchy matter from the infusion by treatment of lead subacetate, removing the excess of lead acetate by treatment with calcium carbonate. The filtrate is then concentrated in order to permit the crystals of salicin to separate out. These are purified by recrystallization. Salicin occurs in shining needles or prisms or as a white crystalline powder melting at 199° to 202° C. It is soluble in about 23 parts of water and about 72 parts of alcohol. As mentioned at the beginning of this chapter, salicin hydrolyzes to saligenin. The latter (p. 714) upon oxidization yields salicylic aldehyde and salicylic acid (p. 800).

Salicin has been synthesized by Kunz, who believes that the graphic formula is:



$$\underbrace{CH_2OH\text{—}CHOH\text{—}\underbrace{CH\text{—}CHOH\text{—}CHOH\text{—}COH}_{O}}_{OC_6H_4CH_2OH}$$

Hirschfelder and his coworkers have synthesized ethers and esters of saligenin which have been found of some value as local anesthetics. They are, however, too pungent and irritating for general use.

Salicin is used as a febrifuge and antirheumatic. It is given in 15-grain doses.

Scutellaria (N.F. VI), or *Skull Cap*, is the dried plant of *Scutellaria lateriflora* Linné (Fam. *Labiatæ*). It contains a glucoside, *scutellarin* and a trace of volatile oil. It is a tonic and is popularly supposed of value as a nervine. Its dose is 15 grains.

Crocus (N.F. VI), or *Saffron*, is interesting as one of the most expensive of vegetable drugs, its great cost being due to the labor of collection.

Saffron consists of the stigma or threadlike floral organs and to obtain a pound of the drug necessitates the picking of stigmas of about 150,000 flowers, and that by hand. Hence, it is easy to understand why saffron is so expensive and why so largely adulterated, the chief adulterant being the shredded petals of other flowers. The chief use of saffron is in domestic practice—for measles—and in cooking.

Saffron contains three crystalline bodies, one of these being *picrocrocin*, a glucoside that hydrolyzes to sativol (chief constituent of the oil), an uncrystallizable lactonic compound, fructose, and formic acid. Its characteristic color is due to a glucosidal pigment called *crocin*, which hydrolyzes to *crocetin*, $C_{17}H_{20}(COOH)_2$, and a carbohydrate, *crocose*.

Convallariæ Radix (N.F. VI), or *Lily-of-the-Valley Root*, is the dried rhizome and roots of *Convallaria majalis*. It contains *convallarin* and *convallatoxin*, glucosides, *convallamarin*, a saponin. It slows and strengthens heart beat, as does digitalis. *Dose.*—0.2 Gm. (3 grains).

Strophanthus (U.S.P. X; N.F. VI) is the dried ripe seed of *Strophanthus Kombé* or *S. hispidus* deprived of its awns. It contains *strophanthin, kombic acid,* a fixed oil, etc. The "awn" referred to in the official definition is a feather-like appendage to the seed, intended to aid in transportation of the seed by the wind.

The fixed oil is a source of annoyance to the pharmacist, as a tincture made with strong alcohol becomes milky when mixed with water. For this reason the official *tincture* is made by first percolating the drug with benzin to remove the fat before percolating with the real menstruum, alcohol. Hatcher does not believe that the fixed oil causes the emetic properties of certain strophanthus preparations.

Note the elaborate requirements set for the biological assay as given in the Formulary. The drug acts upon the heart as does digitalis. *Dose.*—1 grain.

STROPHANTHINUM—Strophanthin

(Strophanthin.

A glucoside or a mixture of glucosides obtained from *Strophanthus Kombé* Oliver (Fam. *Apocynaceæ*).

Strophanthin, when assayed as directed, shall possess a potency equivalent to the activity of not less than 40 per cent and not more than 60 per cent of ouabain when similarly assayed.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White or yellowish powder; very toxic; very soluble in water and in diluted alcohol;

less soluble in dehydrated alcohol; insoluble in chloroform, ether and benzene; dextrorotatory. For details see U.S.P., p. 361.

Color Reactions.—Emerald-green color with sulfuric acid; red-brown, then dark green with ferric chloride and sulfuric acid. See U.S.P.

Extraction.—Strophanthin is obtained by extracting the fat-free pulverized seeds with 70 per cent alcohol, and removing the alcohol from the tincture by distillation. The thin extract after a few days deposits crystals of strophanthin, which after collection on a hardened filter and after recrystallization from boiling water yields a pure product.

It will be seen from the above definition that it is a question whether strophanthin is a definite body or a mixture. Its green color reaction with sulfuric acid is applied not merely to the glucoside but also to microsections of the drug. Inferior species of the drug give with sulfuric acid colors other than green. It is used like strophanthus, but in very minute doses.

Dose.—$\frac{5}{10}$ mg. ($\frac{1}{120}$ grain).

Ouabain is the glucoside obtained from *Strophanthus gratus*. It derives its name from the fact that it was first isolated from the plant *Acokankera Ouabaio*. It is now called G strophanthin and since crystalline is frequently used as the standard in physiological assays of strophanthus.

SCILLA—Squill

(Scill.—Scillæ bulbus P.I.)

Squill consists of the cut and dried fleshy inner scale of the bulb of the white variety of *Urginea maritima* (Linné) Baker (Fam. *Liliaceæ*), known in commerce as White Squill.

Storage.—Preserve in well-closed containers and in a dry place.

Constituents.—Scillitin, $C_{17}H_{25}O_6$, and scillidiuretin. Scillipicrin and scillitoxin are now known to be mixtures. Squill contains calcium oxalate in peculiar-shaped crystals called *raphides,* and also sinistrin and mucilage.

Scillaren is the name given to a mixture of the total glucosides of squill.

Remarks.—While squill is used as a domestic remedy, it must be borne in mind that its active principles have action on the heart similar to digitalis. Hence squill preparations should be used with caution. By reason of the irritating action of its calcium oxalate crystals, ground red squill has been recommended as a rat poison.

Medical Properties.—Nauseant, expectorant, and diuretic.

Official Preparations.—The *vinegar* (p. 277), the *syrup,* made from the vinegar (p. 221), and the *tincture* (p. 251). The *fluidextract* (p. 270) and the *compound syrup* (p. 221) are recognized in the National Formulary.

Dose.—100 mg. ($1\frac{1}{2}$ grains). U.S.P. XI gives no dose.

DIGITALIS—Digitalis

(Digit.—Foxglove, Digitalis folium P.I.)

Digitalis is the dried leaf of *Digitalis purpurea* Linné (Fam. *Scrophulariaceæ*).

The potency of digitalis shall be such that 0.1 Gm. of it, when assayed as directed, shall possess an activity equivalent to not less than 1 U.S.P. digitalis unit. One *United States Pharmacopœial Digitalis Unit* is identical in potency with the *International Digitalis Unit,* as adopted in 1928 by the Permanent Commission on Biological Standardization of the Health Organization of the League of Nations. One *International Digitalis Unit* represents the activity of 0.1 Gm. of the "International Standard Digitalis Powder.'

Digitalis contains not more than 8 per cent of moisture, not more than 2 per cent of stems, browned leaves, flowers, or foreign organic matter, and yields not more than 5 per cent of acid-insoluble ash.

Note.—When digitalis is prescribed, Digitalis Pulverata is to be dispensed.

Storage.—Preserve under all conditions of storage and transportation in waterproof and air-tight containers.

DIGITALIS PULVERATA—Powdered Digitalis

(Digit. Pulverat.)

Digitalis, dried at a temperature not exceeding 60° C. and reduced to a fine powder. Powdered digitalis contains not more than 5 per cent of moisture.

The potency of powdered digitalis shall be such that 0.1 Gm. of it, when assayed as directed, shall possess an activity equivalent to not less than 1 and not more than 1.1 U.S.P. digitalis units. Powdered digitalis of a higher potency is to be reduced to the official standard by admixture with the exhausted marc remaining when preparations of digitalis have been prepared, the marc being dried and finely powdered.

Note.—When digitalis is prescribed, Digitalis Pulverata is to be dispensed.

Storage.—Preserve in water-proof and air-tight containers and protected from light.

Constituents.—*Digitonin* (a saponin), *digitalin* (a glucoside), *digitalein* (mixture of several bodies, chiefly digitonin), *digitoxin*, *gitalin*, *digitophyllin*, *digitin*, digitoflavine, fat (5 per cent), 2 saponins (gitin and digitsaponin) and a substance darkening with ferric chloride and which is a compound of caffeic acid.

Among other constituents, mentioned during the past decade, are *gitoxin*, *gitonin*, *tiogenin*, and *bigitalin*. Burn (1932) expresses the opinion that the only pure constituents of digitalis are digitoxin, digitalin, gitoxin, and digoxin, a glucoside from *D. lanata*.

Among other constituents, mentioned during the past decade, are *gitoxin*, *gitonin*, *tiogenin*, and *bigitalin*. Burn (1932) expresses the opinion that the only pure constituents of digitalis are digitoxin, digitalin, gitoxin, and digoxin, a glucoside from *D. lanata*.

Hatcher finds on shaking infusion of digitalis with chloroform that the chloroform extracts a "digitalis body" that exerts the typical cardiac action of the drug. McGill thinks that this "digitalis body" is a mixture containing digitoxin.

Remarks.—There has been no drug concerning which there have been more conflicting opinions expressed during the past thirty years than digitalis. In truth, about the only fact upon which all observers agree is that it is one of the most valuable drugs in our materia medica. Among the points concerning which opinion has changed we find that while it was for many years thought that digitalis leaves collected from a plant two years old were better than those picked from a young plant, Worth Hale has shown by physiological tests that the first year leaves have as much activity as have those from the two-year-old plant. Again it was supposed that the plucked leaves deteriorated quickly and in some of the foreign Pharmacopœias elaborate directions are given for drying the fresh leaves and for keeping the desiccated leaves dry. Hatcher has shown, however, that old indifferently preserved leaves have as much activity as have those which have been carefully dried. It has also been shown that there is little difference in the activity of wild and cultivated leaves.

It will be seen from the mention of the constituents given above that the chemistry of digitalis is very complex, and is not yet fully cleared up. The confusion is particularly noted in the various digitalins found in the market—the so-called "French digitalin," of Nativelle; that of Homolle; and the commercial "German digitalin," being totally different bodies. The last consists practically of digitonin, and is of but little activity (dose, ⅒ to ½ grain); while Homolle's is quite potent (dose,

$\frac{1}{200}$ to $\frac{1}{40}$ grain). Digitoxin is now considered a more important heart tonic than the several digitalins just described (dose, $\frac{1}{240}$ to $\frac{1}{60}$ grain). The confusion of these digitalins is apt to lead to dangerous results, and until the question is definitely settled on a basis of scientific exactness, the prescribing of digitalin is not to be advised.

The difficulty in selecting digitalis of uniform quality is enhanced by the fact that there is no reliable chemical assay for the drug. Recourse is, therefore, had to a "*physiologic assay*," and as this is the first drug considered in this book where such assay is used, a few words explanatory of such assays may be of service. Physiologic assays are those in which the activity of the drug is tested upon animals, and in each case where employed the method of procedure varies with the drug under consideration. Thus, digitalis is usually tried on frogs, the amount necessary to stop the heart being taken as the factor. Ergot is given to roosters, the quantity needed to produce a certain purple tint of the comb being the gauge of activity. Of course, the tests are far more complex than this scant explanation implies, for example, other factors, such as weight of animal, enter into the calculation leading to standardization.

When we turn to the subject of the pharmaceutical preparations, we find more doubts. As mentioned above it was formerly considered that the heart tonic effect was due to digitalin, which was found in larger amounts in the tincture than in the infusion; while the diuretic action was due to digitonin, which was exhibited in the best form in the infusion. At present, however, there are serious doubts as whether there is any material difference in the action of the tincture and the infusion.

During the past decade, medical authorities of the world have endeavored to place the therapeutics of digitalis upon a scientific basis. In the first place, these authorities have adopted an *International Digitalis Unit* representing the activity of 0.1 Gm. of the "International Standard Digitalis Powder." Then the Commission on Biological Standardization of the League of Nations has formulated a carefully prepared method of biological assay. And lastly, the U.S.P. Revision Committee has introduced into the new Pharmacopœia a monograph on powdered digitalis carefully specifying the biological requirements of digitalis of proper therapeutic strength. For details see U.S.P., pp. 136 and 137.

Medical Properties.—As "cardiac tonic," that is, it slows and strengthens the heart beat and constricts the blood vessels. Of peculiar value in dropsy because of its diuretic action. The *tincture* (U.S.P. XI) and the *infusion* (N.F. VI) are official.

Dose.—100 mg. ($1\frac{1}{2}$ grains).

Lappa (N.F. VI), or *Burdock Root*, is the dried root of *Arctium lappa* Linné, or of other species of *Arctium* (Fam. *Compositæ*), collected from plants of the first year's growth. It is supposed to contain a glucoside, of which but little is known, also mucilage and inulin. Krantz has utilized the carbohydrates of lappa as a diabetic food. Note that the roots of plants of the natural order *Compositæ* usually contain inulin (p. 705) instead of starch. The phrase "from plants of the first year's growth" employed above means that the plant, like digitalis, is a biennial and that the root is collected in the fall of the first year, when filled with the inulin, destined to serve as nourishment for the young shoots of the second year. Lappa is used as a purgative in 30-grain doses.

Capsella Bursa Pastoris, or *Shepherd's Purse*, a familiar European weed enjoyed considerable medical vogue in Germany during the World War. A number of active constituents were ascribed to it, including the glucoside, *hyssopin*, and also hesperidin (p. 714). It was recommended as a substitute for ergot.

Bryony (N.F. VI), the roots of *Bryonia dioica*, is used as an irritant hydragogue cathartic. It contains a neutral principle, $C_{20}H_{30}O_5$; an amorphous glucoside; a phytosterol, $C_{27}H_{46}O$; an alcohol, *bryonal*, $C_{22}H_{34}O_2(OH)_2$, and fat acids. *Dose.*—15 grains.

Jalapa (U.S.P. X; N.F. VI), or *Jalap*, is the dried tuberous root of *Exogonium Jalapa.* It contains 9 per cent of total resin, consisting chiefly of two glucosides, *jalapin* (ether soluble) and *convolvulin* (insoluble in ether); *sugar*, *starch*, etc.

Power and Rogerson have found that resin of jalap contains fatty acids, a phytosterol $C_{27}H_{40}O$, cetyl alcohol, a body $C_{18}H_{36}O$, a glucoside ipurganol, $C_{29}H_{42}O_2(OH)_2$, methyl esculetin, and convolvulinic acid, $C_{15}H_{30}O_3$. The glucosides mentioned above are combinations of the substances just stated. Votocek, on the other hand, claims that convolvulin is a glucoside hydrolyzing to methyl-ethyl acetic acid, convolvulic acid and purginic acid. Convolvulic acid, in turn, hydrolyzes to convolvulolic acid, dextrose, rhodeose and rhamnose; while purginic acid is supposed to split into decylenic acid, hydroxylauric acid, and isorhodeose. Before such conflicting views, the average student can only stand in awe. It is used as a hydragogue cathartic and is administered as *resin* (p. 306), the *fluidextract*, the *compound powder*, and the *tincture*. The resin in a constituent of compound cathartic pills (p. 340) and *pills of colocynth and jalep* (p. 341). *Dose.*—1 Gm. (15 grains).

Ipomœa (U.S.P. X; N.F. VI), or *Orizaba jalap*, or *Mexican scammony*, is the dried root of *Ipomœa orizabensis*. It contains resin, gum, etc.

During the World War the importations of scammony became almost *nil* and scammony substitutes had to be employed. So satisfactory was ipomœa for this purpose, that U.S.P. X replaced scammony root with ipomœa root. Now it has been relegated to the Formulary. The resin obtained from ipomœa resembles fairly closely the scammonin of scammony root.

Ipomœa is used as a hydragogue cathartic. The *resin* (p. 306) is recognized by the Formulary. It is a constituent of *compound extract of colocynth* (p. 303).

Dose.—1 Gm. (15 grains)

Scammony Root (U.S.P. IX) is the root of *Convolvulus Scammonia*. It contains gum, resin, etc. The resin, commonly called *scammonin*, is an extremely complex mixture of glucosides and methyl pentosides of jalapinolic acid, $C_{15}H_{30}(OH)COOH$ and of its methyl ester. According to Power and Rogerson scammonin is similar to but not identical with the resin of ipomœa. Both of these resins are distinctly different from the jalapin of official jalap. Power and Rogerson urge that such words as "scammonin" and "jalapin" should be dropped, as these substances are not distinct chemical entities but are complex mixtures. Scammony root is used as a hydragogue cathartic in 250-mg. doses.

Colocynthis (U.S.P. X; N.F. VI), or *Bitter Apple*, is the dried pulp of the unripe but full-grown fruit of *Citrullus Colocynthis*. It contains two purgative resins, $C_{22}H_{36}O_2(OH)_2$; *hentriacontane*, $C_{31}H_{64}$, a phytosterol, etc. Colocynth pulp is practically the colocynth apple of the former Pharmacopœia except for the fact that the percentage of seed and of epicarp (or rind) is carefully specified. It moreover should not yield more than 6 per cent of acid-insoluble ash. It is used as a hydragogue cathartic. The Formulary recognizes the *extract* (p. 303) and the *compound extract* (p. 303). It is used in a number of N.F. pills.

Dose.—0.125 Gm. (2 grains).

Kamala (N.F. VI), or *Rottlera*, is the hairs obtained from the capsules of *Mallotus philippinensis*. It is used as a tapeworm expeller and as a veterinary vermifuge.

Dose.—For humans, 8 Gm. (2 drachms). For fowls, 0.5 to 1 Gm. (8–15 grains).

Uva Ursi (U.S.P. X; N.F. VI), or *Bear Berry*, is the dried leaf of *Arctostaphylos Uva-ursi*. It contains *arbutin*, a glucoside (originally called *ursin*); *ericolin*, a glucoside; *ursone*, a lactone, isomeric with caryophyllin (see p. 848); *ursolic acid*, $C_{30}H_{48}O_3$; tannic and gallic acids, gum, etc. Arbutin is of interest since it has been made synthetically from its hydrolysis products. (See p. 715.)

It might be mentioned in passing that the Greek name of the plant (arctostaphylos), and the Latin (and specific) name (uva ursi) both mean the same thing; namely, *bear berry*, which is the English synonym. Uva ursi is used as an astringent and diuretic. It is antiseptic to the urinary passages. The *fluidextract* and the *compound fluidextract* are recognized by the Formulary.

Dose.—2 Gm. (30 grains).

Chimaphila (N.F. VI), or *Pipsissewa*, is the dried leaves of *Chimaphila umbellata* (Linné) Barton (Fam. *Ericaceæ*). It contains *chimaphilin*, $C_{24}H_{21}O_4$, and another *glucoside*, $C_{10}H_9O$. These two bodies are not clearly known, but it may be stated that the constituents of the drug are very similar to uva ursi. It is used like the latter drug in 30-grain doses.

Quillaja (N.F. VI), or *Soap Bark*, is the dried bark of *Quillaja Saponaria* Molina (Fam. *Rosaceæ*), deprived of the periderm. It is the first of the "saponinoid" drugs to be considered—drugs containing saponin, an acrid principle which froths in water like soapsuds. All liquid preparations of such drugs froth when agitated. Soap bark is used more for washing colored silk (white fabrics are stained brown yellow by its decoctions) than for pharmaceutic purposes. It is, however, used in making emulsions, for which it would be excellent were it not dangerous on account of its irritating properties.

"Gum foam" used in soda water syrups is a preparation of soap bark. The use of it and similar saponin preparations in beverages is now prohibited in several States.

Ground soap bark should be handled with care, as its dust is very irritating to the nostrils, producing violent sneezing. Such drugs are said to be sternutatory.

SARSAPARILLA—Sarsaparilla
(Sarsap.)

Sarsaparilla is the dried root of *Smilax medica* Chamisso et Schlechtendal, known in commerce as Mexican sarsaparilla; or of *Smilax officinalis* Kunth, or of an undetermined species of *Smilax* known in commerce as Honduras or Ecuadorian sarsaparilla; or of *Smilax ornata* Lemaire, known in commerce as Central American or Jamaica sarsaparilla (Fam. *Liliaceæ*).

Sarsaparilla contains not more than 2 per cent of foreign organic matter, other than the rhizome and crown portion. Mexican sarsaparilla contains not more than 10 per cent of rhizome and stem portion, and yields not more than 4 per cent of acid-insoluble ash. See U.S.P., page 473.

Constituents.—*Parillin* (a glucoside similar to saponin, originally called *pariglin*); *saponin; sarsasaponin;* starch; calcium oxalate in the form of raphides, etc.

According to Power and Salway, Jamaica sarsaparilla contains sarsasaponin, $C_{44}H_{76}O_{20}7H_2O$, and *sitosterol glucoside*, $C_{33}H_{56}O_6$. They consider parillin as a mixture of saponin and a phytosterolin. Kaufmann and Fuchs working on Honduras sarsaparillin isolated two saponins, which upon hydrolysis, yielded a sapogenin, $C_{26}H_{42}O_3$, identical with the substance obtained by Power and Salway from Jamaica sarsaparilla.

Medical Properties.—*Sarsaparilla* is a drug whose reputation is chiefly false. It is vaunted to the skies by the numerous patent medicine men as the greatest of all blood purifiers, yet cold, calm analysis shows it to have but little merit. It contains saponinoid principles which cause it to froth, and possibly a trace of volatile oil, but neither of these can be regarded as great alteratives, and we are forced to the conclusion that its reputation has been gained by its association with other valuable alteratives. It is rarely prescribed by itself, its only simple official preparation being the *fluidextract* (p. 266). The *compound syrup*, U.S.P. XI (p. 221), and the *compound fluidextract*, N.F. VI (p. 270), contain such alteratives as guaiacum and mezereum, and, moreover, these preparations are usually prescribed with potassium iodide.

Dose.—No dose is given in U.S.P. XI. U.S.P. IX fixed the dose at 2 Gm. (30 grains).

Senega (U.S.P. X; N.F. VI), or *Seneca Snakeroot*, is the dried root of *Polygala Senega*. It contains *senegrin* or *polygalic acid* (a form of saponin), a trace of volatile oil, pectin, etc.

The pectin of senega is a source of annoyance in the pharmaceutic preparations of the drug, these gelatinizing or becoming cloudy on standing, due to conversion of the pectin into the insoluble calcium pectate. This decomposition is prevented by the addition of alkali; hence the official senega preparations contain ammonia water.

Senega is an expectorant. It is nauseant and emetic in large doses. The *fluidextract* is official in the Formulary.

Dose.—1 Gm. (15 grains).

BIBLIOGRAPHY

Glucosides.—(Classfication) Rosenthaler, A.Ph.A., 56, 1908, 402.

Hydrolysis of Glucosides.—Amygdalin) Caldwell and Courtauld, Jl. Ch. Soc., 91, 1907, 666; Fischer, B., 28, 1895, 1508; Schimmel, A.Ph.A., 58, 1910, 377; Feist, Arch. d. Pharm., 246, 1908, 206; Herissey, Arch. d. Pharm., 245, 1907, 463; Walker and Krieble, Jl. Ch. Soc., 95, 1909, 1369; Rosenthaler, Arch. d. Pharm., 248, 1910, 534. (Arbutin) Hlasiwetz and Habermann, A.Ph.A., 23, 1875, 440; Stoeder, Jl. Soc. Ch. Ind., 6, 1887, 676. (Convallarin) Lindner, C.A., 9, 1915, 1760. (Digitalin) Kiliani, B., 31, 1898, 2461 and Arch. d. Pharm., 252, 1914, 26; Kiliani and Bazlen, Arch. d. Pharm., 232, 1894, 334; Windaus and co-workers, B., 57B, 1924, 1386; B., 58B, 1925,

1515; B., 61B, 1928, 1847 and 2436; B., 62B, 1929, 475; C.A., 23, 1929, 394 and 843; Burn, Ph. Jl., 129, 1932, 474. (Digitonin) Kiliani, B., 23, 1890, 1555 and 24, 1891, 339; Windaus and Weil, C.A., 16, 1922, 3893. (Digitoxin) Kiliani, B., 31, 1898, 2457 and B., 55B, 1922, 88; Kobert, Ap. Zt., 27, 1912, 555; Cloetta, C.A., 15, 1921, 707; Windaus and co-workers, B., 61B, 1928, 2436; C.A., 23, 1929, 394; Jacobs and Gustus, C.A., 23, 1929, 149; Hasenfratz, C.A., 25, 1931, 1949; Burn, Ph. Jl., 129, 1932, 474. (Gentiopicrin) Kromayer, Arch. Pharm., 160, 1862, 27; Tanret, Compt. rend., 141, 1905, 207. (Glycyrrhizin) Tschirch and Cederberg, Arch. d. Pharm., 245, 1907, 97; Galassi, C.A., 22, 1928, 385. (Ipuranol) Power and Salway, Jl. Ch. Soc., 103, 1913, 399. (Myronic acid) Gadamer, Arch. d. Pharm., 235, 1897, 44. (Salicin) Pyria, A., 56, 1845, 37; Hudson and Paine, Jl. Am. Ch. Soc., 31, 1909, 1242. (Solanin) Heiduschka and Sieger, Jl. ph. ch., 16, 1917, 382. (Strophanthin) Feist, Ap. Zt., 15, 1900, 469. (Chiratin) Flückiger and Höhn, Ph. Jl., 3, 1, 1870, 106. (Colocynthin) Henke, Arch. d. Pharm., 221, 1883, 200. (Convallarin and convallamarin) Walz, A.J.P., 31, 1859, 577. (Ericolin) Thal, A.J.P., 55, 1883, 468. (Hesperidin) Tunmann, Pharm. Cent., 56, 1915, 135. (Parillin) Flückiger, Arch. d. Pharm., 210, 1877, 532. (Scammonin) Klimenko and Raudalin, B., 26, 1893, R 591; Poleck, Arch. d. Pharm., 232, 1894, 315.

Glucosidal Syntheses.—Michael, B., 14, 1881, 2097; Lenz, Ap. Zt., 29, 1914, 128; Mannich, Arch. Pharm., 250, 1912, 547; Bourquelot and co-workers, Jl. ph. ch., 14, 1916, 225; 16, 1917, 353; 19, 1919, 169; 20, 1919, 136; Ph. Jl., 98, 1917, 375; Ch. and Dr., 91, 1919, 1025; Ph. Jl , 105, 1920, 490; Schneider and Sepp, Jl. ph. ch., 15, 1917, 288; Karrer, *ibid.*, 15, 1917, 288; Fischer, Yearbook A.Ph.A., 6, 1917, 448 and 8, 1919, 539; Haworth and Campbell, Jl. Soc. Ch. Ind., 43, 1924, 546 and 691B.

Saponins.—Kobert, Jl. Ch. Soc., 64, 1893, 424 and Ph. Jl., 86, 1911, 245 and 293; Van der Haar, Arch. d. Pharm., 251, 1913, 217; C.A., 11, 1917, 1412; C.A., 16, 1922, 3639 and C.A., 23, 1929, 856; Ruzicka and co-workers, C.A., 23, 1929, 856 and 5189; C.A., 26, 1932, 3244; Windaus and co-workers, C.A., 21, 1927, 589; Poethke, Ph. Zent., 71, 1930, 753; Dafert, C.A., 25, 1931, 2171; Aoyana, C.A., 25, 1931, 1533; Grendel, Ph. Weekbl., 68, 1931, 610; Wasicky, *ibid.*, 12, 1931, 217; Winterstein, C.A., 25, 1931, 5171; Kotake, C.A., 26, 1932, 1627.

Glycyrrhiza.—(History and Collection) Beal and Lacey, Jl. A.Ph.A., 18, 1929, 145; Houseman and Lacey, Jl. Ind. Eng. Ch., 21, 1929, 915; Lloyd, A.J.P., 101, 1929, 805; Anon., Jl. Ind. Eng. Ch. News Ed., 7, March 20, 1929, 9. (Constituents) Tschirch and Cederberg, Arch. d Pharm., 245, 1907, 97; Tschirch and Gauchmann, Arch. d. Pharm., 246, 1908, 545 and 247, 1909, 121; Houseman, A.J.P., 88, 1916, 97; Linz, Arch. Pharm., 254, 1916, 134; Karrer and co-workers, Jl. Soc. Ch. Ind., 40, 1921, 194A; Emmanuel, C.A., 22, 1928, 3486; Houseman and Swift, A.J.P., 101, 1929, 679.

Ammoniated Glycyrrhizin.—(Manufacture) Roussin, A.J.P., 40, 1876, 371; Appenzeller, A.Ph.A., 26, 1878, 613. (Uses) Anon., Ch. and Dr., 26, 1884, 158.

Gentian.—(General) Redgrove, Ph. Jl., 122, 1929, 374. (Constituents) Leconte, A.J.P., 9, 1837, 333; Ludwig and Kromeyer, Dr. Circ., 7, 1863, 91; Hlasiwetz and Habermann, A., 175, 1875, 62; Kostanecki and Tambour, B., 27, 1894, R, 190; Tremann and Mueller, B., 14, 1881, 1988; Hemmelmayr, C.A., 3, 1909, 2687; Meyer, A.Ph.A., 30, 1882, 378; Bourquelot and Bridel, Jl. ph. ch., 22, 1920, 241; Haworth and Wylam, Jl. Soc. Ch. Ind., 42, 1923, 1139; Morner, C.A., 16, 1922, 2522. (Gentianose and Gentiobiose) Berlin, Jl. Am. Ch. Soc., 48, 1926, 1107; Pictet and George, C.A., 20, 1926, 1221; Bridel and Desmarest, C.A., 23, 1929, 5544; Taylor and Lifschitz, J. Am. Ch. Soc., 54, 1932, 1054. (Drying) Bourquelot and Bridel, A.Ph.A., 58, 1910, 184; Schw. Wsch. Ch. Ph., 50, 1912, 279 and 350.

Glycerinated Elixir of Gentian.—Cliffe, A.J.P., 70, 1898, 201.

Chirata.—(Constituents) Flückiger and Hohn, Ph. Jl., 3, 1, 1870, 105; Ram, C.A., 25, 1931, 2807. (Properties) Anon., A.J.P., 12, 1840, 20.

Salicin.—(History) Anon., Jl. ph. ch., 19, 1919, 429. (Extraction) Peschier, A.J.P., 2, 1830, 337. (Synthesis) Kunz, Jl. Am. Ch. Soc., 48, 1926, 262; Helferich and Gootz, B., 65B, 1932, 407. (Saligenin and its esters) Jensen and Hirschfelder, Jl. Soc. Ch. Ind., 44, 1925, 262B.

Scutellaria.—(Constituents) Myers and Gillespie, A.J.P., 61, 1889, 555; Molisch and Goldschmidt, A.Ph.A., 50, 1902, 1065; Bargellini, C.A., 9, 1915, 2237; Wessely and Moser, C.A., 24, 1930, 5038.

Saffron.—(History) Clarke, Ph. Jl., 3, 17, 1887, 1032. (Cultivation) Anon., A.Ph.A., 23, 1875, 136; Koch, Ph. Era, 48, 1915, 57; Anon., Pharm. Era, 53, 1920, 336; Stoneback, Proc. P.P.A., 47, 1924, 148. (Constituents) Pfyl and Schertz, A.Ph.A., 57, 1909, 157; Martini, Bull. Soc. Pharm. Bordeaux, 54, 1914, 136; Decker, Arch. d. Pharm., 252, 1914, 139; Winterstein, C.A., 16, 1922, 2503; Tschirch, *ibid.*, 16, 1922, 2962; Pierlot, C.A., 20, 1926, 797; Karrer and Salomon, C.A., 22, 1928, 2949 and 4464; Lutz, C.A., 25, 1931, 110. (Tests) Wirth, A.J.P., 101, 1929, 716.

Convallaria.—(History) Lloyd, Midland Dr., 45, 1911, 175; Podolsky, Pract. Dr., 50, Oct. 15, 1932, 10. (Constituents) Walz, A.J.P., 31, 1859, 577; Reichard, A.Ph.A., 59, 1911, 504; Karrer, C.A., 23, 1929, 3772.

Strophanthus.—(History) Lloyd, Bull. Pharm., 35, 1911, 242; Sharp, Ph. Jl., 96, 1916, 347. (Extraction) Samaan, Ch. and Dr., 91, 1919, 802. (Constituents) Fraser, Ph. Jl., 3, 20, 1889, 328 and 335; Heiduschka and Wallenreuter, Arch. d. Pharm., 252, 1914, 704. (Tests) Gilg, C.A., 13, 1919, 3272 and Ph. Cent., 61, 1920, 66. (Pharmacology) Hatcher, Jl. A.Ph.A., 5, 1916, 157.

Strophanthin.—Brauns and Closson, Jl. A.Ph.A., 2, 1913, 604, 715 and 843; Jacobs and co-workers, C.A., 18, 1924, 2169; C.A., 20, 1926, 3013; C.A., 22, 1928, 1131; C.A., 23, 1929, 151; 25, 1931, 4888; C.A., 26, 1932, 5958; Thoms and Unger, 18, 1924, 3251.

Ouabain.—Catillon, Jl. ph. ch., 16, 1917, 180.

Squill.—(History) Sharp, Ph. Jl., 84, 1910, 136 and 170; Podolsky, Pract. Dr., 50, Oct. 15, 1932, 10. (Collection) Greenish, Ph. Jl., 105, 1920, 284. (Constituents) Kopaczewski, Ap. Zt., 29, 1914, 847; Riche and Rémont, A.J.P., 52, 1880, 550; Buschmann, Jl. ph. ch., 21, 1920, 364; Home-Morton, Jl. Soc. Ch. Ind., 45, 1926, 851; Stoll, Dr. Circ., 73, 1929, 198; Rosenthaler and Kohli, Jl. Soc. Ch. Ind., 50, 1931, 653B; Anon., Jl. A.M.A., 94, 1930, 1760 and 1761. (Pharmacology) Joz, C.A., 19, 1925, 3317; Henrijean and Kopaczewski, C.A., 20, 1926, 3332.

Digitalis.—(History) X-Rayser II, Ch. and Dr., 77, 1910, 860; Anderssen, Sch. Ap. Zt., 53, 1915, 233; Anon., Pract. Dr., 37, Sept., 1919, 41; Sharp, Ph. Jl., 96, 1916, 347; Kramer, A.J.P. 118, 1936, 264. (Constituents) Kiliani, B., 23, 1890, 1555; B., 24, 1891, 339; Arch. d. Pharm., 234, 1896, 481; and B., 31, 1898, 2454 and B., 59B, 1926, 2462; Finnemore, Ph. Jl., 86, 1911, 489; Wood, A.J.P., 80, 1908, 107; Kraft, Arch. d. Pharm., 250, 1912, 118; Kobert, Ap. Zt., 27, 1915, 555; Kiliani, Yearbook A.Ph.A., 6, 1917, 189 and 192; B., 55B, 1922, 88; Githins, Jl. A.Ph.A., 9, 1920, 1060; McGill, Jl. Am. Ch. Soc., 40, 1920, 1893; Samaan, Ch. and Dr., 94, 1921, 850; Windaus and Brandt, B., 56B, 1923, 2001; Peacock, A.J.P., 96, 1924, 875; Windaus and co-workers, B., 57B, 1924, 1386; Jl. Soc. Ch. Ind., 44, 1925, 566B; C.A., 19, 1925, 1861; B., 58B, 1925, 1515; C.A., 21, 1927, 299; C.A., 23, 1929, 394, 844 and 3230; B., 61B, 1928, 1847; Peacock, A.J.P., 96, 1924, 875; Cloetta, C.A., 20, 1926, 2724; Jacobs and co-workers, C.A., 23, 1929, 4225; Science, 70, 1929, 640; Quart. Jl. Ph., 3, 1930, 659; C.A., 25, 1931, 4888; Bourcet and Fourton, Jl. Soc. Ch. Ind., 48, 1929, 957B; Rapp, Ph. Jl., 123, 1929, 369; Hatcher and Haag, Jl. A.Ph.A., 18, 1929, 551 and 670; Smith, C.A., 25, 1931, 708; Vaudin, Jl. de ph. et ch., [8], 11, 1930, 197; Hasenfratz, C.A., 25, 1931, 1949; Fischer and Schropp, Arch. Pharm., 269, 1931, 157; Burns, Ph. Jl. 129, 1932, 474. (Preservation) Haag and Hatcher, A.J.P., 101, 1929, 474. (Standardization) Hale, Pract. Dr., 29, 1911, 41; Wood, A.J.P., 82, 1910, 101; Hatcher and Brodie, A.J.P., 82, 1910, 360; Knafflenz, C.A., 21, 1927, 301; Tiffeneau, Schw. Apoth. Ztg., 66, 1928, 465; Runne, Ph. Zent., 70, 1929, 453 and 469; Burn and co-workers, Jl. Soc. Ch. Ind., 48, 1929, 112B; Rowe, Jl. A.Ph.A., 18, 1929, 1138; Pichot, Jl. de ph. et ch., [8], 13, 1931, 183. (Pharmacology) Hatcher and co-workers, A.J.P., 57, 1914, 517 and 607; Jl. A.M.A., 75, 1920, 460; Jl. A.Ph.A., 8, 1919, 913 and 12, 1923, 26; Bastedo, Ann. Clin. Med., 5, 1927, 993; Weese, C.A., 23, 1929, 909; McCrea, Science, 69, 1929, 628; Frommel, C.A., 23, 1929, 3739; Nyary, C.A., 26, 1932, 1028; Hoekstra, C.A., 26, 1932, 2241 and 2507.

Lappa.—(Constituents) Wechler, A.J.P., 59, 1887, 393; Hendershott, A.Ph.A., 36, 1888, 344; Shinoda, C.A., 23, 1929, 4707 and 24, 1930, 1387; Krantz and Carr, Jl. Phys. Ch., 35, 1931, 756.

Capsella Bursa Pastoris.—Oesterle, Jl. Soc. Ch. Ind., 42, 1923, 70A; Arny, Proc. N. Y. S. Ph. A., 43, 1921, 62; Wander, C.A., 20, 1926, 799.

Bryony.—Power and Moore, Jl. Ch. Soc., 99, 1911, 937.

Jalap.—(Production) Anon., Pharm. Era, 53, 1920, 75. (Constituents) Power and Rogerson, Jl. Am. Ch. Soc., 32, 1910, 80; C.A., 7, 1913, 2932; Votocek, B., 43, 1910, 476 and C.A., 23, 1929, 2719; Asahina and Akasu, C.A., 20, 1926, 365; Hollander, C.A., 20, 1926, 1862; Adams and Davies, Jl. Am. Ch. Soc., 50, 1928, 1749; Peyer and Rosenthal, C.A., 24, 1930, 683.

Scammony.—(Constituents) Poleck, A.J.P., 64, 1892, 465; Power and Rogerson Jl. Ch. Soc., 101, 1912, 398. (Extraction) Briggs, Nat. Dr., 51, 1921, 194.

Ipomœa Root.—Power and Rogerson (see above).

Colocynth.—(Constituents) Power and Moore, Jl. Ch. Soc., 97, 1910, 99; Votocek and Valentin, C.A., 22, 1928, 1361; Peyer and Rosenthal, C.A., 24, 1930, 683. (Properties) Sechler, Am. Dr., 57, 1910, 336.

Uva Ursi.—(Constituents) Meissner, A.J.P., 2, 1831, 339; Kawalier, A.J.P., 25, 1853, 68; Hughes, A.J.P., 19, 1847, 88; Jungmann, A.J.P., 43, 1871, 202; Trommsdorff, A.J.P., 27, 1855, 334; Thal, A.J.P., 55, 1883, 468; Lewin, Ph. Jl., 3, 14, 1883, 940. (Arbutin) Michael, B14, 1881, 2097; Bourquelot and Bridel, Jl. ph. ch., 27, 1908, 421; Bayliss, Jl. Physiology, 43, 1911, 455; Mannich, Arch. d. Pharm., 250, 1912, 547; Rosenthaler, Ph. Acta Helv., 4, 1929, 55; Apoth. Zt., 45, 1930, 1081. (Ursone) Dodge

Jl. Am. Ch. Soc., 40, 1918, 1917; Nooyen, Ph. Week., 47, 1920, 112; Van der Haar, C.A., 18, 1924, 2511; Dodge, Jl. Am. Ch. Soc., 52, 1930, 1722; Sando, C.A., 25, 1931, 2151.

Chimaphila.—(Constituents) Beshore, A.J.P., 59, 1887, 125; Peacock, A.J.P., 64, 1892, 295.

Quillaja.—(Sources) Nicoresti and Tallantyre, Ph. Jl., 105, 1920, 95. (Constituents) Harry and Boutron-Charlard, A.J.P., 12, 1840, 209; Bolley, A.J.P., 27, 1853, 43; Kobert, Am. Dr., 17, 1888, 72; Kofler, C.A., 18, 1924; 2209. (Use in drinks) Ladd, Dr. Circ., 59, 1915, 345; White, Pure Food Jl., 10, 1915, 589.

Sarsaparilla.—(History) Manwaring, Science, 70, 1929, 1. (Pharmacognosy) Apt, Ber. dtsch. Pharm. Ges., 31, 1921, 155. (Constituents) Palotta, Jl. d. Ph., 10, 1824, 543; Flückiger, Ph. Jl., 3, 8, 1877, 488; Kobert, A.J.P., 64, 1892, 465; Power and Salway, Jl. Ch. Soc., 105, 1914, 201; Kaufmann and Fuchs, B., 56B, 1923, 2527; Van der Haar, C.A., 23, 1929, 5472.

Senega.—(Constituents) Quevenne, Jl. d. Ph., 22, 1836, 449; Procter, A.Ph.A., 8, 1859, 297; Bolley, A.J.P., 27, 1855, 43; Rosenthaler, B. ph. Ges., 22, 1912, 261; Wedekind and Krecke, B., 57B, 1924, 1118; Dafert and Kalman, Quart. Jl. Ph., 3, 1930, 659. (Gelatinization of preparations) Kennedy, A.J.P., 27, 1879, 721.

CHAPTER XLI

DERIVATIVES OF THE HIGHER HYDROCARBONS

FATS, SOAPS, AND WAXES

As already mentioned, chain hydrocarbons containing more than six carbon atoms are known. Thus we have heptane, C_7H_{16}; octane, C_8H_{18}; nonane, C_9H_{20}; decane, $C_{10}H_{22}$, and likewise the bodies $C_{11}H_{24}$, $C_{12}H_{16}$, and so on to $C_{60}H_{122}$. Many of the members of the series are found in petroleum.

Heptane, C_7H_{16}, is found in the volatile oil of *Pinus sabiniana*. Kremers reports it as a solvent possessing unusual qualities.

Heptyl aldehyde or *œnanthol* is prepared from castor oil. By oxidation with permanganate, it is converted into œnanthic acid, $CH_3CH_2CH_2CH_2CH_2CH_2COOH$.

Ethyl œnanthylate the ester of this acid is a liquid of characteristic and agreeable odor that makes it useful in preparing grape and other fruit essences.

Octane, C_8H_{18}, is now prepared commercially from the proper petroleum distillate. The normal form is a colorless liquid, boiling at 125° C. and has the specific gravity, 0.706. Some 23 isomeric octyl alcohols are known.

Nonane, C_9H_{20}, can be prepared from castor oil. Nonyl aldehyde has been used as an adulterant of oil of rose.

Duodecane, $C_{12}H_{26}$, yields an aldehyde which is used in perfumery.

Hexadecane, $C_{16}H_{34}$, yields a series of alcohols having the formula $C_{16}H_{33}OH$. One of these hexadecyl alcohols is known as *cetyl alcohol* or *æthal*, and is interesting as the alcoholic part of the ester which is the chief constituent of spermaceti. Cetyl alcohol yields on oxidation *palmitic acid*, $C_{15}H_{31}COOH$, which is the common constituent of fats and waxes. Thus *cetin*, the chief constituent of spermaceti, is the ester, *cetyl palmitate*.

Likewise the palmitate of glyceryl, commonly known as *palmitin*, is a common constituent of fats.

Octodecane, $C_{18}H_{38}$, yields the alcohol $C_{18}H_{37}OH$ (or $C_{17}H_{35}CH_2OH$) and this upon oxidation yields *stearic acid*, $C_{17}H_{35}COOH$.

ACIDUM STEARICUM—Stearic Acid

(Acid. Stearic.)

A mixture of solid acids obtained from fats, and consisting chiefly of palmitic acid [$CH_3(CH_2)_{14}COOH$] and stearic acid [$CH_3(CH_2)_{16}COOH$].

Summarized Description.

Hard white or yellowish-white, somewhat glossy, solid; odorless or faint tallow odor; soluble in about 17 parts of alcohol; insoluble in water; soluble in chloroform, ether, carbon disulfide or carbon tetrachloride; melts at not lower than 54° C. Iodine number, not more than 4; ash, not more than 0.1 per cent. For details, see U.S.P., p. 27.

For *tests for identity* and for *impurities* (neutral fat or paraffin, mineral acids), see U.S.P., p. 27.

Remarks.—Stearic acid is a white, waxy solid, insoluble in water, melting at 70° C. when pure. The commercial acid, however, has a much lower melting point. Its commercial source is solid fats, such as tallow and suet, which, on treatment with superheated steam, yield glycerin and stearic acid. Hence most commercial stearic acid is a side product in glycerin manufacture.

Tallow and suet are composed chiefly of *stearin* or the stearic acid ester of glycerin, and this, like all esters, can be easily decomposed by treatment with an alkali or with superheated steam by the following reaction:

$$C_3H_5(C_{18}H_{35}O_2)_3 + \underset{\text{Steam}}{3H_2O} = C_3H_5(OH)_3 + 3HC_{18}H_{35}O_2.$$

At present, however, considerable stearic acid is made by the "hydrogenation" of oleic acid. (See next page.)

Stearic acid is official because it enters into the manufacture of glycerin suppositories, a very small quantity of stearic acid soap being ample to solidify a large quantity of glycerin. It is largely used in the cosmetic, soap, and rubber industries.

Thus in the U.S.P. recipe, 92 Gm. of glycerin are solidified by heating with 8 Gm. of sodium stearate and 5 Gm. of distilled water; the products of the reaction being glyceryl stearate and sodium stearate.

Margaric acid is a name applied to pearly scales isolated from some fats by Chevreul. Its analysis shows the formula $C_{16}H_{33}COOH$. There has been considerable controversy as to whether this acid really exists or whether it is merely a mixture of palmitic and stearic acid. Lately a definite glyceryl margarate has been produced synthetically. This has been given the name *Intarvin* and is recommended as the fatty food for diabetic patients.

ACIDUM OLEICUM—Oleic Acid

(Acid. Oleic.)

A liquid acid obtained from tallow and other fats, and consisting chiefly of $CH_3(CH_2)_7CH{:}CH(CH_2)_7COOH$.

Storage.—Preserve in well-closed glass or stoneware containers and in a cool place.

Summarized Description.

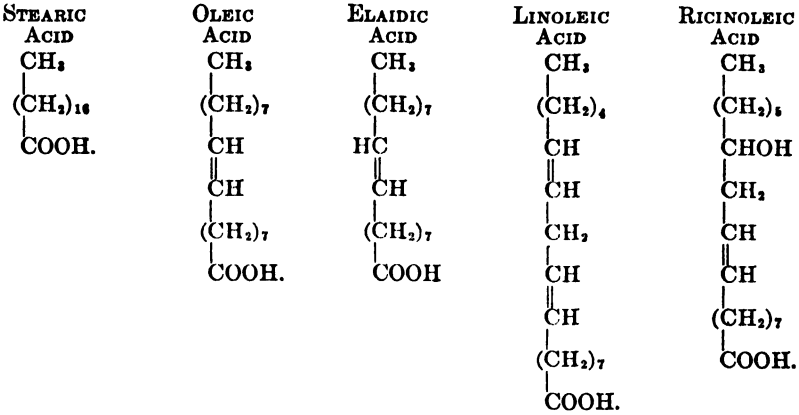
Yellowish or brownish-yellow oily liquid; peculiar lardlike odor and taste; free from rancidity; insoluble in water; miscible with alcohol, chloroform, benzene, petroleum benzin and in fixed and volatile oils; sp. gr. 0.895; congealing point, not more than 10° C.; decomposes upon heating. For details, see U.S.P., p. 24.

For *impurities* (stearic acid, undecomposed fats, mineral oil, mineral acids), see U.S.P., p. 24.

Remarks.—Oleic acid is obtained from oils by treating same with superheated steam in the process of glycerin manufacture. For making oleates, one should employ a very pure form of oleic acid made by treating a solution of castile soap with diluted sulfuric acid.

Oleic acid is the product of unsaturated hydrocarbon $C_{16}H_{36}$, and as can be noticed, it represents stearic acid minus 2 atoms of hydrogen.

The best comparison of this body with stearic acid and with other similar acids can be made by representing the structural formulas side by side:



Stearic Acid: $CH_3-(CH_2)_{16}-COOH$.

Oleic Acid: $CH_3-(CH_2)_7-CH=CH-(CH_2)_7-COOH$.

Elaidic Acid: $CH_3-(CH_2)_7-HC=CH-(CH_2)_7-COOH$

Linoleic Acid: $CH_3-(CH_2)_4-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$.

Ricinoleic Acid: $CH_3-(CH_2)_5-CHOH-CH_2-CH=CH-(CH_2)_7-COOH$.

There are 16 possible isomeric forms of oleic acid and 15 of these may exist in their stereo-isomeric form of elaidin acids. Of these 11 oleic and 3 elaidic acids have been described by Fahrion.

Oleic acid is a yellow or yellowish-brown, oily liquid, not affecting litmus paper, and solidifying at 4° C.

On treatment with a large quantity of alcoholic potassium hydroxide it breaks into palmitic and oxalic acids. Strong heat with nitric acid breaks it up into a number of simpler bodies; on the other hand, gentle heat with nitric acid converts it into the isomeric yellow solid *elaidic acid,* the graphic formula of which is given above.

Oleic acid is the chief constituent of liquid fats or oils in the form of the glycerin ester *olein.*

The oleic acid solutions of metallic oxides or alkaloids form the pharmaceutic class, oleates (p. 234).

Hydrogenation of Oils.—By treating the unsaturated oleic acid (or oleates) with hydrogen in the presence of a catalytic agent, like finely divided nickel, solid saturated stearic acid (or stearates) are produced. At present there are more liquid fats available than solid ones and hydrogenation has solved the problem of supplying solid fats. Partial hydrogenation furnishes semisolid fats used as lard substitutes, while complete hydrogenation yields products as hard as beef tallow.

Hydrogenated oils have been suggested as useful ointment bases.

Behenic acid, $C_{21}H_{43}COOH$, was obtained originally from oil of ben, an oil expressed from the seed of *Moringia pterygospermum.* Oil of ben is *not* benne oil, which is a synonym for sesame oil. At present behenic acid is made synthetically by the reduction of *erucic acid* (obtained from rape seed oil) with hydrogen iodide. An intermediate step in this process is *monoiodobehenic acid,* $C_{21}H_{42}ICOOH$, the calcium salt of which is known as *calioben* and *sajodin,* while the iron salt is sold under the trade name *ferioben.* Upon the bromination of behenic acid, *dibrombehenic* acid is obtained. The calcium salt of the latter acid is known as *sabromin* or *calbroben.*

CALCII IODOBEHENAS—Calcium Iodobehenate

(Calc. Iodobehen.—Calcium Monoiodobehenate)

Calcium Iodobehenate consists principally of calcium monoiodobehenate $[C_{21}H_{42}ICOO)_2Ca]$ and contains, when dried to constant weight at 100° C., not less than 23.5 per cent of I.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White or yellowish, unctuous powder; odorless or faintly fatlike; insoluble in water; slightly soluble in alcohol and ether; soluble in warm chloroform. (See U.S.P., p. 101).

For *tests for identity* and for *impurities* (carbonate, magnesium and alkali salts, soluble salts, chloride, sulfate) and for *assay*, see U.S.P., p. 101.

Remarks.—This official chemical is now enjoying considerable vogue as an organic iodine preparation producing less gastric disturbances than ordinary iodides.

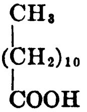
Dose.—500 mg. (8 grains).

Linoleic acid, $C_{17}H_{31}COOH$, differs from oleic acid by possessing 2 atoms of hydrogen less. It is, therefore, more unsaturated than oleic acid. In the form of glycerin ester it is the chief constituent of linseed oil, the drying properties of which render it so valuable in paint. Most oils spread on wood and are absorbed by the fibers, leaving a permanent greasy stain; with linseed oil, on the other hand, the stain gradually becomes resinous, due to the oxidation of linolein into the product linoxyn. Very similar to it are the other acids of linseed oil, *linolenic acid* and *isolinolenic acid.* In fact, there still wages a controversy as to whether the last two are not merely impure forms of linoleic acid.

Ricinoleic acid, $C_{17}H_{32}OHCOOH$, represents oleic acid, in which one hydrogen has been replaced by a hydroxyl group. It, in the form of glycerin compound, is the chief constituent of castor oil. Ricinoleic acid forms a chemical combination with sulfuric acid, and the product which is generally obtained by direct treatment of castor oil with sulfuric acid forms with potassa a jelly-like liquid which, on account of its excellent solvent powers, has been called "polysolve." It dissolves a variety of substances, as metallic salts, gums, resins, solid extracts, iodoform, and chrysarobin.

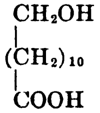
Other fat and wax acids are:

LAURINIC ACID



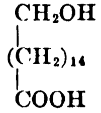
$CH_3-(CH_2)_{10}-COOH$

SABINIC ACID



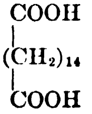
$CH_2OH-(CH_2)_{10}-COOH$

JUNIPERIC ACID



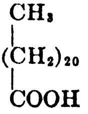
$CH_2OH-(CH_2)_{14}-COOH$

THAPSIC ACID



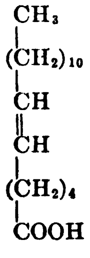
$COOH-(CH_2)_{14}-COOH$

BEHENIC ACID



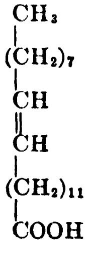
$CH_3-(CH_2)_{20}-COOH$

PETROSELINIC ACID



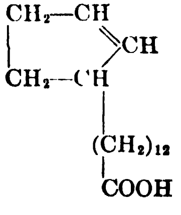
$CH_3-(CH_2)_{10}-CH=CH-(CH_2)_4-COOH$

ERUCIC ACID



$CH_3-(CH_2)_7-CH=CH-(CH_2)_{11}-COOH$

CHAULMOOGRIC ACID



OILS AND FATS

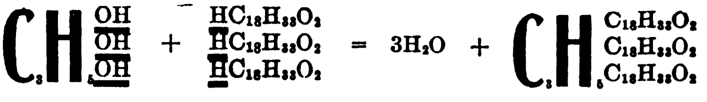
An oil is any liquid which greases—which leaves, when dropped on cloth, a stain which water will not wash out, a stain which makes paper translucent. If a solid substance exhibits similar properties, it is called a fat. Oils are called *volatile* or *fixed,* according as this stain disappears on warming or is permanent by reason of the nonvolatility of the oil—characters clearly defined by the names given the two groups.

Fixed oils and fats are usually combinations of glycerin with oleic, stearic, palmitic, or analogous acids—are glycerin esters of these acids.

As already learned (p. 637), alcohols react with acids, just as do the inorganic basic hydroxides, and such products of alcohols called esters are analogous to the inorganic salts. Among examples of such ester formation already cited were:

$$C_2H_5OH + HNO_2 = H_2O + C_2H_5NO_2 \text{ Ethyl nitrite.}$$
$$C_2H_5OH + HC_2H_3O_2 = H_2O + C_2H_5C_2H_3O_2 \text{ Ethyl acetate.}$$

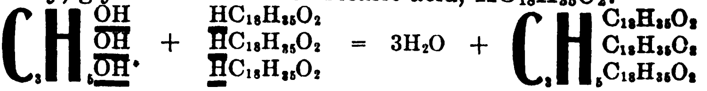
Similarly, glycerin reacts with acids forming esters. Thus, 1 molecule of glycerin, $C_3H_5(OH)_3$, reacts with 3 molecules of oleic acid, $HC_{18}H_{33}O_2$, as shown graphically below:



$$C_3H_5\begin{matrix}OH\\ \underline{\overline{OH}}\\ \underline{OH}\end{matrix} + \begin{matrix}HC_{18}H_{33}O_2\\ \overline{H}C_{18}H_{33}O_2\\ \underline{H}C_{18}H_{33}O_2\end{matrix} = 3H_2O + C_3H_5\begin{matrix}C_{18}H_{33}O_2\\ C_{18}H_{33}O_2\\ C_{18}H_{33}O_2\end{matrix}$$

or $C_3H_5(C_{18}H_{33}O_2)_3$, glyceryl oleate or olein.

Similarly, glycerin reacts with stearic acid, $HC_{18}H_{35}O_2$:



$$C_3H_5\begin{matrix}OH\\ \underline{\overline{OH}}\\ \underline{OH}\end{matrix} + \begin{matrix}HC_{18}H_{35}O_2\\ \overline{H}C_{18}H_{35}O_2\\ \underline{H}C_{18}H_{35}O_2\end{matrix} = 3H_2O + C_3H_5\begin{matrix}C_{18}H_{35}O_2\\ C_{18}H_{35}O_2\\ C_{18}H_{35}O_2\end{matrix}$$

or $C_3H_5(C_{18}H_{35}O_2)_3$, glyceryl stearate or stearin.

Combinations of varying proportions of glyceryl oleate (olein), glyceryl palmitate (palmitin), and glyceryl stearate (stearin) form the fixed oils and fats. The larger the proportion of olein, the more liquid is the fatty substance, oils like that from olives being largely olein. As the amount of stearin increases the more solid the fatty substance becomes, until, in tallow, there is little olein and much stearin.

Fats are prone to decomposition with the production of a disagreeable sour odor. This is called *rancidity*. This is due to the splitting of the fat into glycerin and the fat acids, but the odor is due to either heptyl aldehyde or nonyl aldehyde.

Various preservatives (antioxidants) have been suggested as preventing rancidity. Of these hydroquinone is found the most satisfactory but its pharmaceutical use is advisable only in certain cases.

Fats are now being called *lipins* and similar substances are denominated *lipoids*. Rosenboom and Gies have devised a scientific classification of these bodies. The first group consists of the true lipins, including what we call fatty acids, fats, oils, waxes, and soap; the lipoids, which are far more numerous and more complicated in structure, are classified as proteolipins, glycolipins, phospholipins, sterols, esterols, cholates, etc.

Armstrong and others incline to the belief that the olein, stearin, and palmitin are not found in fats as mechanical mixtures but in molecular combinations, such as palmitodistearin, stearo-dipalmitin, etc.

Fats and fatty oils and waxes are grouped by Allen as follows:

I. Olive oil group: Nondrying vegetable oleins. Examples: Olive, almond, peanut, and mustard oils.

II. Cottonseed oil group: Intermediate between I and III; hence adulterants of both. Examples: Cottonseed, rape seed, beechnut, and sesame oils.

III. Linseed oil group: Containing linoleic acid, hence drying oils, becoming resinous on boiling with litharge. Examples: Linseed oil and a few others.

IV. Castor oil group: Containing ricinoleic and other acids. Examples: Castor, croton, and Japan wood oils.

V. Palm oil group: Semisolid fats. Examples: Palm, theobroma, and nutmeg oils.

VI. Coconut oil group: Solid esters of lauric acid ($C_{11}H_{23}COOH$). Easily saponified, hence valuable in soap making. Example: Coconut oil.

VII. Lard oil group: Animal oleins. Examples: Lard, neatsfoot, and bone oils.

VIII. Tallow group: Solid animal fats. Examples: Tallow, lard, suint, and butter.

IX. Whale oil group: Marine animal oleins, mixed with glycerides of caproic and valerianic acids. Examples: Whale, porpoise, and cod liver oils.

X. Sperm oil group: Liquid waxes, being esters of monatomic alcohols; thus, sperm oil is the oleate of lauric alcohol, $C_{12}H_{25}OH$. Examples: Sperm, bottlenose, and dolphin oils.

XI. Spermaceti group: Waxes, esters of higher monatomic alcohols. Examples: Spermaceti, beeswax, and Japan wax.

Fixed oils and fats are extracted from their natural sources by the several methods described below under the individual oil. Summarized, principal methods are: (*a*) expression; (*b*) warming the comminuted material with water and drawing off the separated oil; (*c*) extraction with a volatile solvent. The crude oil is usually refined by heating with a weakly alkaline solution followed by separation of the solid portion ("foots") by standing or by clarification with absorbents such as suitable clays or by direct filtration.

OLEUM OLIVÆ—Olive Oil

(Ol. Oliv.—Sweet Oil)

The fixed oil obtained from the ripe fruit of *Olea europæa* Linné (Fam. *Oleaceæ*).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Pale-yellow or greenish-yellow oily liquid; slight peculiar odor and taste; slightly soluble in alcohol; miscible with ether, chloroform or carbon disulfide; sp. gr. 0.910 to 0.915; becomes cloudy at 8° to 10° C. and congeals at 0°. For details, see U.S.P., p. 263.

For *tests for identity* and for *impurities* (cottonseed oil, sesame oil), see U.S.P., p. 263.

Saponification Number.—190 to 195. Details in U.S.P.

Iodine Absorption Number.—79 to 88. Details in U.S.P.

Composition.—Olein, 67 per cent; palmitin, 28 per cent; linolein, 5 per cent.

Jamieson and Baughman and also Täufel and Sarria report percentage figures differing from the foregoing. In truth, the composition of the oil depends upon place of growth and method of preparation.

Remarks.—Olive oil is obtained by expressing the ripe olive, the same fruit which, when green and pickled, forms the familiar table relish.

Virgin olive oil is one extracted by cold pressure from selected ripe olives without heat or treatment of any kind except filtration or settling. Its flavor is superior to the so-called "refined" oils and it is less likely to turn rancid.

Formerly olive oil was largely adulterated with cottonseed oil, but two tests have been devised which can readily detect this sophistication. One of these is the Halphen test, the red tint produced when cottonseed oil or its mixtures is digested with a reagent consisting of solution of sulfur in amyl alcohol and carbon disulfide. The other is Becchi's test, which is based upon the blackening of an alcoholic solution of silver nitrate when it is heated on a water with cottonseed oil or its mixtures. Sesame oil is detected by Badouin's test (p. 731).

Thanks to these tests and to the rigid scrutiny of food officials most of the olive oil at present in the American market is pure. It might be well to point out that under Food Decision 139, *sweet oil* means olive oil only.

The last two tests given in the summarized description—the *saponification number* and the *iodine absorption number*—are of great importance in establishing the constants for all fixed oils.

As, however, a clear understanding of the two tests implies a comprehension of the theory of volumetric analysis, explanation of the tests will be left for the chapter on Pharmaceutic Testing (pp. 1023–1026).

Medical Properties.—Laxative and emollient; mildly antiseptic. It is used largely as a basis of liniments.

Dose.—30 cc. (1 fluidounce).

OLEUM AMYGDALÆ EXPRESSUM—Expressed Almond Oil
(Ol. Amygd. Exp.—Oil of Sweet Almond)

Expressed Almond Oil is the fixed oil obtained from the kernels of varieties of *Amygdalus communis* Linné (Fam. *Rosaceæ*).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Clear pale straw-colored oily liquid; bland taste; slightly soluble in alcohol; miscible with ether, chloroform, benzene or petroleum benzin, sp. gr. 0.910 to 0.915. For details, see U.S.P., p. 248.

For *tests for identity,* for *impurities* (olive oil, lard oil, peach kernel oil, apricot kernel oil, sesame oil, cottonseed oil, paraffin oil, foreign oils, peanut oil), see U.S.P., p. 248.

Saponification Number.—191 to 200. Details, see U.S.P.

Iodine Absorption Number.—93 to 100. Details, see U.S.P.

Composition.—Olein, 76 per cent, stearin and palmitin.

Remarks.—The sources of this oil will be studied in other places, sweet almond in this chapter (p. 740) and bitter almond in Chapter XLIII (p. 795). A large amount of the commercial oil of sweet almond is, in reality, the fixed oil expressed from peach and apricot kernels, and in the official data given above will be found a test for distinguishing the true oil from these substitutes.

Medical Properties.—Demulcent and laxative. Used in *cold cream* (p. 365).

Oleum Sesami (N.F. VI), or *Benne Oil* or *teel oil,* is obtained from the seed of *Sesamum indicum.* It consists of the glycerides of oleic, linolic, palmitic, stearic, arachidic and lignoceric acids and *sesamin and sesamolin;* two crystalline bodies. It is used in making *ammonia liniment,* N.F. (p. 743).

The test for identity of this oil, the red color produced by treating the oil with hydrochloric acid containing sugar, was devised by Badouin and is useful for detecting the presence of the oil as an adulterant of olive oil.

OLEUM IODATUM—Iodized Oil
(Ol. Iodat.)

An iodine addition product of vegetable oils, containing not less than 39 per cent and not more than 41 per cent of organically combined iodine (I).

Summarized Description.

Thick viscous oily liquid; alliaceous odor and an oleaginous taste; decomposes on exposure to air and sunshine.

For *test for identity* and for *assay,* see U.S.P., p. 255.

Remarks.—This new official is a fatty oil that has absorbed iodine. That made from poppy-seed oil is called *lipiodol.* While sometimes used as a substitute for inorganic iodides, its chief use is as contrast medium in *x*-ray work.

OLEUM MAYDIS—Corn Oil
(Ol. Mayd.)

The refined, fixed oil expressed from the germ of *Zea Mays* Linné (Fam. *Gramineæ*).

Storage.—Preserve in well-closed containers in a cool place.

Summarized Description.

Clear light yellow oily liquid, faint characteristic odor and taste; slightly soluble in alcohol, miscible with ether, chloroform, benzene and petroleum benzin; sp. gr., 0.914 to 0.921. For details, see U.S.P., p. 258.

For *tests for identity* and for *impurity* (cottonseed oil), see U.S.P., p. 258.

Saponification Number.—188 to 193. For details, see U.S.P.

Iodine Absorption Number.—112 to 128. For details, see U.S.P.

Remarks.—This new official oil is obtained by expression of the germ of corn and is a by-product in the manufacture of cornstarch and glucose (p. 695). It is used in making certain ointments and as a solvent for irradiated ergosterol.

OLEUM GOSSYPII SEMINIS—Cottonseed Oil

(Ol. Gossyp. Sem.—Cottonseed Oil)

Cottonseed Oil is the refined, fixed oil obtained from the seed of cultivated plants of various varieties of *Gossypium herbaceum* Linné or of other species of *Gossypium* (Fam. *Malvaceæ*).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Pale-yellow oily liquid; bland taste; slightly soluble in alcohol; miscible with ether, chloroform, petroleum benzin and carbon disulfide; sp. gr. 0.915 to 0.921; becomes turbid at 12° C.; congeals at 0° to −5° C. For details, see U.S.P., p. 255.

For *tests for identity*, see U.S.P.

Saponification Number.—190 to 198. Details, see U.S.P.

Iodine Absorption Number.—105 to 114. Details, see U.S.P.

Composition.—Olein, palmitin, linolein, and small amounts of the glycerides of stearic, arachidic and myristic acids; phytosterols, etc.

Remarks.—Cottonseed oil, like all other fixed oils, should be "cold pressed," that is, the expression of the oil from the seed should be done between the *cold* plates of a hydraulic press (p. 181). In order to increase the output of their product, oil pressers frequently express the seed between heated plates, in which event the oil contains not only the liquid fats (olein), but also the solid fats, which are melted by the heated plates. Such an oil is a limpid liquid in warm weather, but on cool days it becomes cloudy and unsightly, and its filtration is a tedious task.

Any pharmacist who has regard for his reputation will carefully avoid use of such an oil in making official liniment of camphor (p. 290). Whether an oil is cold pressed or hot pressed can be easily tested by a small vial of it to a cool temperature. It must be borne in mind, however, that the official oil will turn cloudy at a temperature of 12° C.; hence in applying the above test the temperature should not be below that figure.

The conversion of cottonseed oil to an orange semisolid mass by heating with nitric acid in a water bath constitutes the *elaidin reaction.* That is, the olein (glyceryl oleate) of the oil is changed into elaidin, the glycerin ester of elaidic acid, described on p. 727. The same reaction takes place with most fixed oils and fats, notably with lard oil and lard, and has pharmaceutic application in the latter case in the manufacture of citrine ointment.

As mentioned on p. 730, cottonseed oil has been largely used as an adulterant of olive oil but according to custom authorities this practice of adulterating olive oil with cottonseed oil prior to shipment from Italy has become practically obsolete due to the rigid inspections made at American ports of entry.

Cottonseed oil is used in making *camphorated oil* (p. 290).

Medical Properties.—Demulcent and laxative.

OLEUM LINI—Linseed Oil

(Ol. Lini.—Oil of Flaxseed, Raw Linseed Oil)

Linseed Oil is the fixed oil obtained from linseed.

Note.—Linseed oil that has been "boiled" or treated with a drier must not be used or dispensed.

Storage.—Preserve in well-closed containers.

Summarized Description.

Yellowish oily liquid; peculiar odor; bland taste; thickens on exposure to air; slightly soluble in alcohol; miscible with ether, chloroform, petroleum benzin, carbon disulfide or oil of turpentine; sp. gr. 0.925 to 0.935. For details, see U.S.P., p. 258.

For *tests for identity* and for *impurities* (free acid, nondrying oils, mineral or rosin oils, rosin), see U.S.P.

Saponification Number.—187 to 195. See U.S.P.

Iodine Absorption Number.—Not less than 170. See U.S.P.

Composition.—Glycerides of linoleic acid, linolenic acid, isolinolenic acid; oleic acid; phytosterols, etc. Gay also finds 9 to 10 per cent of saturated acids. (See p. 727.)

Remarks.—The official oil is what is commercially termed "raw oil"; that is, the oil just as it emerges from the press. For painting purposes the raw oil is cooked with lead, cobalt or manganese compounds, thereby enhancing its "drying" qualities. Such oil is called "boiled oil," and the pharmacopœial definition given above gives special warning against the use of such boiled oil in medicine. As the boiled oil is more important in commerce than the raw oil, the pharmacist should be sure to specify "raw oil" in buying.

Linseed oil is a "drying oil." It contains, instead of olein, a similar body, *linolein,* which, however, differs from the former by oxidizing to a solid, *linoxyn,* supposedly $C_{57}H_{96}O_{20}$. Hence on being dropped or spread on a board, it eventually hardens into a protective surface, and, accordingly, it and the other drying oils are of value in painting; for which purposes the nondrying oils are unfitted.

It will be noticed among the tests for linseed oil given above that linseed oil is adulterated with mineral oils (various grades of refined petroleum) and with rosin or *rosin oil;* the latter, the product of the destructive distillation of rosin, is rapidly becoming an important article of commerce.

Medical Properties.—Demulcent and laxative. A constituent of *lime liniment,* N.F. (p. 291).

OLEUM RICINI—Castor Oil
(Ol. Ricin.)

Castor Oil is the fixed oil obtained from the seed of *Ricinus communis* Linné (Fam. *Euphorbiaceæ*).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Pale yellowish or almost colorless transparent viscid liquid; faint mild odor; bland, then acrid then nauseating taste; miscible with dehydrated alcohol and with glacial acetic acid: sp. gr. 0.945 to 0.965. For details, see U.S.P., p. 265.

For *tests for identity,* for *impurities* (other fixed oils), see U.S.P., p. 265.

Saponification Number.—179 to 185. Details, see U.S.P.

Iodine Absorption Number.—83 to 88. Details, see U.S.P.

Composition.—Note that the olein of this oil is the glyceryl ester of ricinoleic acid (p. 727).

Remarks.—Castor oil is one of the few fixed oils which is freely soluble in official alcohol. For this reason it is useful as the greasy constituent of hair lotions.

Medical Properties.—Valuable purgative. The only drawback to the administration of the oil is the disgust it usually excites, hence a disguised form is often demanded. The best method of administration is in sarsaparilla soda water, the following points being carefully executed. First, put about 15 drops of compound tincture of cardamom in a clean dry glass, twisting the glass so that its complete interior is moistened with this aromatic. Then add an ounce of regular soda fountain sarsaparilla syrup and squirt in the soda water with the fine stream. Of course this will produce a large amount of foam, and at this juncture pour in the dose of oil, carefully avoiding contact with the sides of the glass. Thus poured in, the oil will float between the bottom layer of the sarsaparilla soda and the foam on top, and, as the mixture is swallowed, the foam first and the soda water last, convey to the tongue and the palate so decided a flavor that the oil slips down almost unnoticed. The compound tincture of cardamom is an essential, as it not only serves to keep the oil from sticking to the glass, but, moreover, by its aromatic odor and taste, does much in disguising the disagreeable odor and taste of the oil.

Castor oil can be solidified by the trituration of an equal amount of magnesium oxide. That the product is not a soap is shown by the fact that most of the oil can be extracted from the powder by treatment with ether. The product, however, is a chemical combination of the two ingredients. The magnesia type of *solid castor oil* enjoyed much popularity some ten years since under trade-marked names.

Dose.—15 cc. (4 fluidrachms).

The so-called "castor oil capsules"—that is, the small ones of hard gelatin holding about 15 minims—are not to be recommended, as their purgative action is due to substances added to the castor oil, such as croton oil or podophyllin.

Aromatic Castor Oil (N.F.) consists of the oil flavored with an alcoholic solution of oil of cinnamon, oil of clove, vanillin and coumarin, in which gluside (saccharin) is also dissolved as a sweetening agent.

Oleum Tiglii (U.S.P. X; N.F. VI), or *Croton Oil,* is a fixed oil expressed from the seed of *Croton Tiglium.* It is a pale yellow or brownish-yellow liquid, which must be handled carefully as it causes blistering of the skin. It contains the glycerides of tiglinic (methylcrotonic), acetic, butyric, valerianic, stearic, palmitic, laurinic, myristic, crotonic, oleic, and formic acids. A resin-like blistering substance, *crotonol,* $C_{30}H_{54}O_9$, is also present. It is a powerful purgative, used only in cases of last resort, when all other purgatives have failed, its action being too violent for general use. It is a vesicant, producing blisters on application to the skin.

It is usually administered internally in the form of pills, the oil being solidified by use of crumb of bread.

Dose.—0.06 cc. (1 minim).

OLEUM THEOBROMATIS—Theobroma Oil

(**Ol. Theobrom.**—Cacao Butter, Cocoa Butter, Oil of Theobroma)

The fat obtained from the roasted seed of *Theobroma Cacao* Linné (Fam. *Sterculiaceæ*).

Storage.—Preserve in a cool place.

Summarized Description.

Yellowish-white solid; faint agreeable odor; bland chocolate-like taste; slightly soluble in alcohol; more so in dehydrated alcohol; freely soluble in ether, chloroform or benzene and petroleum benzin; sp. gr. 0.854 to 0.864; melts between 30° and 35° C. For details, see U.S.P., p. 271.

For *tests for identity* and for *impurities* (wax, stearin or tallow), see U.S.P., p. 271.

Saponification Number.—188 to 195. Details, see U.S.P.

Iodine Absorption Number.—35 to 40. Details, see U.S.P.

Refractive Index.—1.4537 to 1.4578. Details, see U.S.P.

Composition.—Glycerides of oleic, linoleic, lauric, palmitic, stearic, and arachic acids. Matthes and Rhodich also found a phytosterin consisting of amyrilene and two true phytosterins.

Lea (1929) conducted a painstaking study of the composition of cacao butter and reports that it consists essentially of complicated oleo-palmito-stearins (p. 729). It is to these, according to Lea, the characteristic properties of the fat are due.

Remarks.—Oil of theobroma is, chemically and physically, just between the oils and fats. While a hard solid at ordinary temperatures, the heat of the body is sufficient to melt it—to convert it to a liquid. This valuable property suggested to Duhamel in 1842 its use as a basis for suppositories, every other fat melting at so low a temperature being a soft, sticky mass at ordinary temperatures.

Note that the common term "cocoa butter" is replaced in the Pharmacopœia by the more accurate "cacao butter" (the latter word being pronounced as if spelled "ka-ka-o"). This step relieves the confusion arising from the fact that three different plants have been given very similar names. These plants and products are:

Cacao (cocoa) and butter of cacao from *Theobroma Cacao*, the chocolate plant.
Coconut, from *Cocis nucifera*, the coconut palm.
Coca leaves from *Erythroxylon Coca*, the coca shrub.

Hence the necessity of learning to say "cacao," for otherwise one is sure to confound the plant yielding chocolate and oil of theobroma with the coconut palm or with the coca tree.

Medical Uses.—Suppository base. Emollient for chapped hands.

OLEUM CHAULMOOGRÆ—Chaulmoogra Oil
(Ol. Chaulmoog.)

The fixed oil expressed from the ripe seed of *Taraktogenos Kurzii* King, *Hydnocarpus Wightiana* Blume, or *Hydnocarpus anthelmintica* Pierre (Fam. *Flacourtiaceæ*). The fixed oil expressed from the ripe seed of other species of *Hydnocarpus* (Fam. *Flacourtiaceæ*), when designated as such and when conforming with the description, physical properties and tests for identity and purity prescribed below, may be used.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Yellow or yellow-brown liquid; whitish soft solid below 25° C.; characteristic odor; acrid taste; sparingly soluble in alcohol; soluble in benzene, chloroform, ether and petroleum benzin; sp. gr. 0.940 to 0.960; $[\alpha]_D$ of 10 per cent chloroformic solution $+48°$ to $+60°$ C. For details, see U.S.P., p. 251.

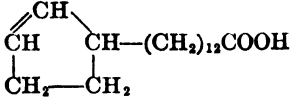
For *tests for identity* and for *impurity* (free acid), see U.S.P., p. 251.

Saponification Number.—196 to 213. Details, see U.S.P.

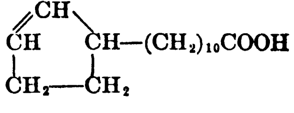
Iodine Absorption Number.—93 to 104. Details, see U.S.P.

Composition.—Glycerol and phytosterol esters of chaulmoogric and hydnocarpic acids. The formulas of these acids are as follows:

Chaulmoogric Acid
$C_{18}H_{32}O_2$



Hydnocarpic Acid
$C_{16}H_{28}O_2$



Hashimoto found beside the two acids just mentioned, *taraktogenic acid*, $C_{30}H_{60}O_6$, *isogadoleic acid*, $C_{20}H_{38}O_2$, a lactone, $C_{18}H_{32}O_2$ and possibly some arachidic acid.

Remarks.—This remedy was dispensed by the writer in 1890–91 on the prescriptions of Dr. Isadore Dyer of New Orleans, one of the pioneers in America in the field of leprosy treatment. It should be noted that while it was originally believed that chaulmoogra oil was obtained from the seed of Gynocardia species, Powers' study showed that gynocardia oil is distinctly different from the official oil.

Medical Uses.—A valuable remedy on leprosy. Recommended in tuberculosis, but its value in this disease is questioned.

Dose.—1 cc. (15 minims).

ÆTHYLIS CHAULMOOGRAS—Ethyl Chaulmoograte (Æthyl. Chaulmoog.)

The ethyl esters of the mixed acids of chaulmoogra oil.
Storage.—Preserve in well-closed containers.

Summarized Description.

Clear pale-yellow liquid; fruity odor; insoluble in water; miscible with alcohol, chloroform and ether; sp. gr. 0.904; $[\alpha]_D$ of 50 per cent chloroformic solution, not less than +44.5° C.

For details, see U.S.P., p. 41.
For *tests for identity* and for *impurity* (free acid), see U.S.P., p. 41.
Saponification Number.—190 to 196. Details, see U.S.P.
Iodine Number.—90 to 100. Details, see U.S.P.

Remarks.—Experiments with patients at a leper hospital in Honolulu showed that intravenous injections of chaulmoogra oil were far more effective than administration by the mouth. Such intravenous injections of the oil or of its separated fatty acids were found inconvenient, if not dangerous and investigators, notably Dean and Wrenshall, endeavored to find safer chaulmoogra preparations. Of these the most satisfactory is the mixed ethyl esters of the chaulmoogric acids; this administered intravenously being now considered as a specific in leprosy.

Dose.—1 cc. (15 minims).

Adams and coworkers (1929) synthesized a number of octodecanoic acids and their esters and found their pharmacological effect resembled the chaulmoogra esters.

Coconut Oil is expressed from *copra,* the dried "meat" of the coconut. It contains the glycerides of caprylic, lauric, myristic, palmitic, stearic, oleic, capronic, capric and linoleic acids. It is a semisolid fat and is used in soap making.

Peanut Oil is largely used as a salad oil. It consists of the glycerides of arachidic, lignoceric, stearic, palmitic, oleic and linoleic acids. It is sometimes used in pharmacy as a basis of liniments.

Soy Bean Oil is expressed from the seed of *Glycine hispida,* the chief foodstuff of the Manchurians. The oil contains of the glycerides of oleic, linoleic, linolenic, palmitic, stearic, arachidic and lignoceric acids. The oil is excellent for soap making and would be of service in pharmacy as a basis of liniments.

Oleum Adipis (U.S.P. VIII), or *Lard Oil,* is a fixed oil expressed from lard at a low temperature. Instead of calling it, as in the case of castor oil, "cold pressed," this cold pressed lard oil is called in commerce "*winter strained,*" the two terms meaning practically the same thing. It consists of olein, some linolein, stearin and palmitin, the amount of solid constituents varying from very little in the best "winter strained" oil to much when the oil has been carelessly pressed.

Lard oil, like linseed oil, is largely adulterated with various petroleum oils. It was chiefly the presence of these mineral oils that made difficult the manufacture of citrine ointment from lard oil as directed by U.S.P. 1890, and for this reason the ointment of the N.F. VI is made from lard.

Tung Oil, or *Chinese Wood Oil,* is obtained from the seed of *Aleurites cordata, A. fordii* and *A. montana.* Its cultivation in Florida began in 1896. It contains the glycerides of linolenic, palmitic and eleostearic acids. It is an essential raw material of present-day varnish manufacture.

Rapeseed Oil is obtained from the seed of *Brassica campestris.* It is used in Europe for making green soap (p. 743). Raiziss and Glaser have used an iodized rapeseed oil under the name campiodol as a diagnostic reagent in *x*-ray work.

Palm Oil is obtained from the kernel of *Elæis guineensis,* the palm tree of West Africa. The oil contains the glycerides of caprylic, capric, lauric, myristic, palmitic, stearic, oleic and linoleic acids. It is used very largely in soap making.

OLEUM MORRHUÆ—Cod Liver Oil (Ol. Morrh.)

The partially destearinated fixed oil obtained from fresh livers of *Gadus morrhua* Linné and other species of the Family *Gadidæ. Cod Liver Oil may be flavored by the addition of not more than 1 per cent of any one or any mixture of flavoring substances recognized* *in this Pharmacopœia.* Cod liver oil contains in each Gm. at least 600 U.S.P. units of Vitamin A and at least 85 U.S.P. units of Vitamin D.*

The Vitamin A potency and Vitamin D potency of cod liver oil when designated shall be expressed in "United States Pharmacopœia Units" per gram of oil and may be referred to as "U.S.P. Units."

Storage.—Preserve in a cool place, in well-closed containers which have been thoroughly dried before filling. Cod liver oil may be bottled or packaged in a vacuum or in the presence of an inert gas.

Summarized Description.

Pale-yellow thin oily liquid; peculiar slightly fishy nonrancid odor; fishy taste; slightly soluble in alcohol; soluble in ether, chloroform, carbon disulfide or ethyl acetate; sp. gr. 0.918 to 0.927. For details, see U.S.P., p. 261.

For *tests for identity*, for *impurity* (free fatty acids) and for *vitamin assay*, see U.S.P., p. 261.

Saponification Number.—180 to 190. Details, see U.S.P.

Iodine Absorption Number.—145 to 180. Details, see U.S.P.

Medical Properties.—Demulcent, nutritive in wasting diseases. Best administered in the form of the official *emulsion* (p. 288).

Dose.—Average daily dose—infants and adults, 8 cc. (2 fluidrachms). Lower doses when Vitamin A and D content exceeds U.S.P. minimum.

OLEUM MORRHUÆ NON-DESTEARINATUM—Non-destearinated Cod Liver Oil

(Ol. Morrh. Non-destearin.)

The entire fixed oil obtained from fresh livers of *Gadus morrhua* Linné and other species of the Family *Gadidæ*, containing not more than 0.5 per cent by volume of water and liver tissue. Non-destearinated Cod Liver Oil contains in each gram at least 600 U.S.P. units of Vitamin A and at least 85 U.S.P. units of Vitamin D.

The Vitamin A potency and Vitamin D potency of Non-destearinated Cod Liver Oil, when designated, shall be expressed in "United States Pharmacopœia Units" per gram of oil and may be referred to as "U.S.P. Units."

Storage.—Preserve in a cool place, in well-closed containers. It may be stored in a vacuum or in the presence of an inert gas.

Manufacture.—The oil is separated from fresh livers either by exposing to sun, when oil exudes; by slowly heating on steam bath; by treating with live steam; or by boiling with water and skimming off the separated oil.

Composition.—Olein, little palmitin and stearin, unsaturated fatty acids, traces bromides and iodides, cholesterin, animal decomposition products (alkaloids) and vitamins (see p. 955).

Remarks.—U.S.P. XI provides for two grades of this important oil. The new type, *non-destearinated cod liver oil*, is a crude oil of the same vitamin content as the medicinal product, differing from the latter chiefly because of permission to contain a small amount of the natural stearin. It is intended primarily to permit manufacturers to import the crude oil for the purposes of refining. A large amount of crude oil is also imported for use in poultry feeding.

The use of cod liver oil as a vitamin-rich medicament has brought demands for a rigidly standardized type of oil; hence the elaborate rubric given above and of the detailed storage directions. The day of poor quality cod liver oil and careless storage of same is now a thing of the past.

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* One "United States Pharmacopœia Unit of Vitamin A" is equal, in growth promoting and antiophthalmic activities for the rat, to one International unit of Vitamin A as defined and adopted by the Conference of Vitamin Standards of the Permanent Commission on Biological Standardization of the League of Nations in June of 1931; one "United States Pharmacopœia Unit of Vitamin D" is equal, in antirachitic potency for the rat, to one International unit of Vitamin D as defined and adopted by the Conference of Vitamin Standards of the Permanent Commission on Biological Standardization of the League of Nations in June of 1931.

Introduced in medicine in 1822, cod liver oil has continued to enjoy popularity as a remedy in cases of malnutrition. Many theories as to its superiority over other oils have been advanced. It was first thought that its iodine content gave the oil its peculiar value; then it was assumed that its unsaturated fatty acids gave it its special properties; then its virtues were ascribed to its "alkaloids" and extracts prepared from the oil and sold as "*gaduol*," "*morrhuol*," etc. were used alone or in the so-called "wine of cod liver oil." Now it is regarded as certain that the therapeutic value of the oil resides in its vitamin (p. 955) content and the new Pharmacopœia provides an assay for Vitamin A formed in the oil.

Sodium Morrhuate is prepared from cod liver oil, the peculiar fatty acid of which is called *morrhuic acid.* Rogers and others have found sodium morrhuate of value in tuberculosis.

Latterly the oil of the livers of the halibut and of the tunny fish have been offered to the medical public under the names *haliver oil* and *tunliver oil* respectively. These are claimed to have a much higher Vitamin A and Vitamin D content than the best grade of natural cod liver oil.

ADEPS—Lard

Lard is the purified internal fat of the abdomen of the hog, *Sus scrofa var. domesticus* Gray (Fam. *Suidæ*).

Storage.—Preserve in a cool place, in well-closed containers which are impervious to fat.

Summarized Description.

Soft white unctuous solid; faint odor; bland taste; free from rancidity; insoluble in water; slightly soluble in alcohol; freely soluble in ether, chloroform, carbon disulfide and petroleum benzin; melts between 36° and 42° C. For details, see U.S.P., p. 34.

For *tests for identity*, for *impurities* (alkalis, chlorides, free fatty acids), see U.S.P., p. 34.

Saponification Number.—195 to 203. Details, see U.S.P.

Iodine Absorption Number.—46 to 70. Details, see U.S.P.

Composition.—Consists of the glycerides of lauric, myristic, palmitic, stearic, oleic, and linoleic acids. The proportion of the acids is approximately 40 per cent of solid acids, 50 per cent of oleic acid, and 10 per cent of linoleic acid.

Remarks.—Note that, according to the rule laid down when discussing fats (p. 729), whether a fat is liquid or solid depends on the relative amount of olein and stearin it contains. Olive oil is almost pure olein; suet, which is hard, is almost pure stearin, while lard, which is half-and-half, is semisolid.

The solid fat of cottonseed oil is used for adulterating lard, and the pharmacopœial test for this impurity is the *Becchi test* mentioned under olive oil. (See p. 730.)

Medical Properties.—Emollient and ointment base. Now used instead of lard oil in making *citrine ointment* N.F. VI (p. 621).

ADEPS BENZOINATUS—Benzoinated Lard

(Adeps Benz.)

Condensed Recipe.

Digest 1000 Gm. lard with 10 Gm. coarsely powdered Siam benzoin and then strain. In warm climates 5 per cent of white wax may be added. For details, see U.S.P., p. 35.

Remarks.—It will be seen that this official is made by digesting ground benzoin in melted lard, and *not* by mixing lard with tincture of benzoin, as the writer has known some indifferent druggists to do. Lard rapidly turns rancid, and the benzoin is added to hinder the decomposition.

SEVUM PRÆPARATUM—Prepared Suet

(Sev. Præp.—Mutton Suet)

The internal fat of the abdomen of the sheep, *Ovis aries* Linné (Fam. *Bovidæ*), purified by melting and straining.

Storage.—Preserve in a cool place, in well-closed containers impervious to fat.

Summarized Description.

White solid fat; nearly inodorous; bland taste; becomes rancid on exposure to the air; insoluble in water and in cold alcohol; soluble in boiling alcohol and in cold ether and petroleum benzin; melts between 45° and 50° C.; congeals between 37° and 40° C. For details, see U.S.P., p. 333.

For *tests for identity* and for *impurity* (free acid), see U.S.P., p. 333.

Saponification Number.—193 to 200. Details, see U.S.P.

Iodine Absorption Number.—33 to 48. Details, see U.S.P.

Composition.—Stearin and palmitin, 70 per cent; olein, 30 per cent; *hercin*, a trace. Hilditch also finds myristic and linoleic acids.

Remarks.—Suet turns rancid even more rapidly than lard. Borrell found that when melted suet was digested with elm bark the resulting "*ulmated suet*" kept quite well.

ADEPS LANÆ—Wool Fat

(Adeps Lan.—Anhydrous Lanolin, Refined Wool Fat)

Wool Fat is the purified, anhydrous, fatlike substance from the wool of sheep, *Ovis aries* Linné (Fam. *Bovidæ*).

Storage.—Preserve in a cool place, in well-closed containers which are impervious to fat.

Summarized Description.

Brown-yellow tenacious, unctuous mass; only slight odor; insoluble in but miscible with about twice its weight of water; sparingly soluble in alcohol; freely soluble in ether and in chloroform; melts between 38° and 42° C. For details, see U.S.P., p. 36.

For *tests for identity*, for *impurities* (water, alkalis and soaps, free alkalis and free acids, chlorides, glycerin, soluble oxidizable matter, petrolatum), see U.S.P., p. 36.

Iodine Absorption Number.—18 to 36. Details, see U.S.P.

Manufacture.—Crude suint (the alkaline washings from sheep wool) is treated with acid, thereby liberating the fatty acid combination of cholesterin and isocholesterin, and also 30 per cent free fatty acid. The fatty mixture is then treated with caustic alkali, which saponifies the free fats and emulsifies the cholesterin compounds. The mixture is centrifuged, when the cholesterin compounds separate as cream and are thus removed from bad-smelling fatty acids.

Composition.—A mixture of the esters of oleic, stearic, palmitic, cerotic, caproic, butyric, and isovaleric and myristic acids with the cholesterins and some ceryl alcohol. It contains no glyceryl compounds as do most fats. Lewkowitsch points out that this substance is more like a wax than a fat. In fact, he calls it *wool wax.*

Remarks.—The fat of sheep wool has already been considered as *suint*, under the head of the Potassium Salts (p. 458).

Purified suint was introduced in modern medicine under the copyrighted name *lanolin*, and since its introduction has enjoyed great popularity, because of the fact that it is more readily absorbed by the pores of the skin than lard or other fats.

It readily absorbs water, and when combined with 30 per cent of that fluid, it forms the official *hydrous wool fat.*

ADEPS LANÆ HYDROSUS—Hydrous Wool Fat

(Adeps Lan. Hyd.—Lanolin)

Hydrous Wool Fat contains not less than 25 per cent and not more than 30 per cent of water.

Storage.—Preserve in a cool place, in well-closed containers which are impervious to fat.

Summarized Description.

Yellowish-white, or nearly white, ointment-like mass; insoluble in but miscible with water; gives turbid solutions with ether and chloroform; loses 25 to 30 per cent of water on evaporation on a water bath. For details, see U.S.P., p. 36.

For *tests for identity* and for *impurities*, see Wool Fat.

Manufacture.—Made by melting wool fat, gradually adding 30 per cent warm water, and triturating until cool.

Medical Properties.—Emollient and ointment base. Twelve official ointments are made with one of the two forms of wool fat.

Eucerin, or *Aquaphor,* is an ointment base obtained from wool fat, possessing a much greater water-absorbing capacity than has lanolin; it being capable of taking up seven to eight times its own weight of water. After the saponifiable fatty acids are removed from the crude suint as described under wool fat, from the cholesterin mixture by selective extraction can be separated a body consisting of a mixture (or soft fat) consisting of the esters of isocholesterol and oxycholesterol with oleic, myristinic and carnaubic acids. To this soft fat, petrolatum hydrocarbons are added as diluents and the product is marketed under the trade-marked name.

DRUGS CONTAINING FIXED OILS

Fixed oils are usually found in the seed of plants, although there are some exceptions. Thus butternut bark (juglans, N.F. V) contains appreciable quantities of fixed oil. In many official seeds, such as strophanthus (p. 717), the fixed oil is of importance only because its presence is a source of annoyance in making pharmaceutic preparations; hence in this chapter we will discuss only those drugs that owe their entire therapeutic value to the fixed oil they contain.

The **mustards** (white or black) will be considered under the thiocyanates (p. 753), since their activity is due to their sulfurated volatile oils.

Bitter almond will be considered under *benzaldehyde,* since its active principle, the volatile oil, is composed chiefly of that body.

Amygdala Dulcis (U.S.P. IX), or *Sweet Almond,* is the seed of *Prunus Amygdalus dulcis.* It contains 59 per cent of fixed oil (*oleum amygdalæ expression,* U.S.P.); 24 per cent of albumin; the enzyme *emulsin*; and asparagin. Since sweet almond contains not more than traces of the glucoside amygdalin (p. 713) or of volatile oil, no hydrocyanic acid odor is produced on moistening the seed, even though the enzyme, emulsin, is present. Almonds are *blanched* by removing the scurfy seed coat. This is accomplished by immersing them in hot water for a few minutes, when the coat can be easily slipped off. Whatever medical value sweet almond possesses is because of its demulcent properties. It is used in *emulsion of almond,* U.S.P. IX (p. 287).

LINUM—Linseed

(Flaxseed)

Linseed is the dried ripe seed of *Linum usitatissimum* Linné (Fam. *Linaceæ*).

Linseed contains not more than 2 per cent of other seeds or foreign organic matter, and yields not less than 30 per cent of nonvolatile, ether-soluble extractive, at least 98 per cent of which is saponifiable.

Summarized Description.

The meal must be free from rancid odor; a 2 per cent decoction of a fat-free sample must not give more than a faint blue color with iodine; meal must yield at least 30 per cent of oil on extraction with petroleum ether and, of this, at least 98 per cent must be saponifiable. For details, see U.S.P., p. 203.

Constituents.—Fixed oil, 30 per cent (*oleum lini,* U.S.P.); mucilage, 6 per cent (*d*-galactonic acid plus *l*-rhamnose); albumin; sugar, linamarin (like amygdalin), etc.

Remarks.—It is difficult to decide whether flaxseed should be grouped among the mucilaginous or the oleaginous drugs.

The unbroken seed is used, because of the mucilage, while in the ground seed both the oil and the mucilage play a therapeutic rôle. The mucilage of the seed is interesting, as being found entirely in the outer layer of cells; hence by immersing the whole seed in water all the mucilage is extracted.

Much of the ground flaxseed of commerce is the seed deprived of part or all of its oil; hence the pharmacopœial test given above requiring at least 30 per cent of oil.

Linseed contains some starch, but not large amounts, and thus differs from most of the adulterants of the ground seed. This explains the pharmacopœial test for "limit of starch."

Medical Properties.—The mucilage (also the unground seed) is demulcent. Therefore an infusion of the whole seed is used as a basis of domestic cough mixtures, while a thicker solution is sometimes used as a bandolin or as a face jelly, although for this purpose quince seed or tragacanth is more useful. Ground seed mixed with hot water to thick paste forms the familiar "*flaxseed poultice.*"

Pepo (U.S.P. X), or *Pumpkin Seed*, contains 20 to 40 per cent of fixed oil, sugar, starch and resin. The oil consists of linolein, olein, palmitic and stearin; while the resin is a combination of a phytosterol ($C_{27}H_{46}O$) with hydroxycerotic acid. It is popularly considered as a tenifuge, but Power and Salway after an exhaustive examination of the drug report their inability to find any ingredient that would be likely to expel tapeworm. Sollman's pharmacological researches, however, show that pumpkin seed is an efficient anthelmintic. *Dose.*—30 Gm. (1 ounce).

Watermelon Seeds, from *Cucurbita citrullus*, have long been used in folk medicine in the south as a diuretic. Althausen and Kerr (1929) find that the seeds contain a glucoside-saponin, *cucurbocitrin*, which is of distinct value in the treatment of high blood pressure.

LYCOPODIUM—Lycopodium

(Lycopod.)

Lycopodium consists of the spores of *Lycopodium clavatum* Linné (Fam. *Lycopodiaceæ*).

Lycopodium yields not more than 0.75 per cent of acid-insoluble ash.

Constituents.—Fixed oil, 43 per cent consisting of lycopod-oleic (hexadecenoic), dihydroxy-stearic, palmitic, and myristic acids.

Remarks.—The official definition of lycopodium is "the spores of *Lycopodium clavatum*," etc. The spores of nonflowering plants are organs midway between the fruit and the seed of flowering species, though there is a decided difference in the way the two sprout into new plants.

The large quantity of oil contained in lycopodium accounts for its mobility—its smooth, slippery character—as well as causing the remarkably quick combustion of lycopodium when blown into a flame. It is very difficult to extract the oil from lycopodium, as it is next to impossible completely to break the walls of the individual cell which forms each sporule. By long contusion with sand the result may be reached.

Because of its mobility it is called "*witch powder*" in some sections of the country.

Medical Properties.—Externally, as a dusting powder. Its use as a dusting powder for pills has been already given.

Castor Beans are the seed of *Ricinus communis*. Besides the oil (see p. 733) castor beans contain ricinin, $C_7H_9O_2N_2$ and a frightfully poisonous enzyme, ricin (see p. 955). The presence of this enzyme makes castor bean distinctly toxic.

SOAPS

Soaps are products resulting from the action of sodium and potassium hydroxide on oils or fats. All the ingredients employed in commercial soap making are more or less impure, hence the products are not definite chemical compounds.

The Pharmacopœia recognizes as soap—*sapo durus*—made from olive oil and soda—and *sapo mollis*—from linseed oil and potassa. Fixed oils are combinations of the oleate, stearate, and palmitate of glyceryl. If we take glyceryl oleate and treat it with sodium hydroxide we get a reaction quite similar to that occurring when fat is treated with steam (p. 678), namely:

$$\underset{\substack{\text{Olein}\\\text{(Glyceryl oleate.)}}}{C_3H_5(C_{18}H_{33}O_2)_3} + \underset{\substack{\text{Sodium}\\\text{hydroxide}}}{3NaOH} = \underbrace{\underset{\text{Glycerin}}{C_3H_5(OH)_3} + \underset{\text{Sodium oleate.}}{3NaC_{18}H_{33}O_2}}_{\text{Soap.}}$$

SAPO DURUS—Hard Soap

(Sapo Dur.—Sapo U.S.P. X, Soap)

Soda soap.

Storage.—Preserve in well-closed containers.

Summarized Description.

White or nearly white solid, in bars or a yellowish-white powder; faint characteristic odor, free from rancidity; disagreeable alkaline taste; soluble in alcohol and water; alkaline to indicators. For details, see U.S.P., p. 325.

For *tests for identity*, for *impurities* (water, soap from animal fats, heavy metals, sodium chloride, sodium carbonate, silica, alkali hydroxides, free fatty acids, alkali carbonates), see U.S.P., p. 325.

Iodine Absorption Number.—(Of the separated acids) 83 to 92. Details, see U.S.P.

Remarks.—Soap is a product of the treatment of an oil, supposedly olive oil, with sodium hydroxide. Now much commercial soap is made by direct treatment of fatty acids with sodium carbonate. Soap, U.S.P., was formerly called "Castile soap," because originally made in the ancient kingdom of Castile, Spain, and at the present time the finest brand of Castile soap on the market is the "Yaritu" brand manufactured in that district. A large proportion of the so-called "Castile soap," however, is manufactured in Marseilles, while a number of American soaps made from fats other than olive oil now masquerade as "Castile" soap.

Made by the usual method, Castile soap is a mixture of glycerin and sodium oleate. The red Castile soap is colored by the addition of ferrous oxide, which is black, and this, on exposure to air, is oxidized to red ferric oxide—iron rust. The effect can be noticed by making a fresh cut through a cake of mottled Castile soap, which shows on the interior black streakings which, on exposure to air, gradually assume the red hue of the rest of the soap. The coloring (or mottling) is simply to please the eye, as the ferric oxide is of no influence, save to increase weight.

Soap is used chiefly externally, although it is sometimes administered internally as a laxative, especially in purgative pills. For this purpose it is used in *pills* of *aloes* (U.S.P.) and of *asafetida* (N.F.).

An alcoholic solution of soap containing camphor and oil of rosemary is official as *camphor and soap liniment* (p. 291).

SODII STEARAS—Sodium Stearate

(Sod. Stear.)

A mixture of sodium stearate ($NaC_{18}H_{35}O_2$) with varying proportions of sodium palmitate ($NaC_{16}H_{31}O_2$).

***Storage.*—Preserve in well-closed containers and protected from light.**

Summarized Description.

Fine white powder, soapy to touch, usually having a tallow-like odor; slowly soluble in cold water and in alcohol. For details, see U.S.P., p. 348.

For *tests for identity* and for *impurities* (alcohol-insoluble substances, free alkali, free fatty acids), see U.S.P., p. 348.

Remarks.—This new official has been introduced into U.S.P. XI, because it is used in making *glycerin suppositories* (p. 357). It is made by heating a solution of sodium carbonate with stearic acid on a water bath, adding a small amount of alcohol and then dissolving the completed stearate in hot water. This aqueous solution is then "salted out" by addition of sodium chloride and sodium carbonate.

SAPO MOLLIS—Soft Soap

(Sapo Moll.)

Condensed Recipe.

Dissolve 19.1 Gm. potassium hydroxide or about 46.3 Gm. sodium hydroxide in water, warm, mix with 400 Gm. linseed oil, boil, stir, add 50 cc. glycerin and saponify by heat. For details, see U.S.P., p. 326.

Summarized Description.

Soft unctuous yellowish-white to brownish-yellow mass; slight characteristic odor; alkaline taste; solution is alkaline to litmus and to phenolphthalein; 97 per cent should be soluble in hot alcohol; should contain from 0.1 to 0.25 per cent of free potassium hydroxide, and not more than 52 per cent of water. For details, see U.S.P., p. 326.

Remarks.—Soft soap is made from linseed oil and potassium and sodium hydroxides and clearing the product with an appropriate quantity of glycerin. *Green soap* is a soft soap originally made with potassa and greenish hemp seed oil.

The two soaps (hard and soft) are interesting as illustrating the different actions of the salts of two metals. The sodium salts are usually efflorescent and, similarly, Castile soap is found to effloresce on standing. The potassium compounds, like potassa soap, are deliquescent.

Soft soap is used externally in skin troubles, and is a constituent of the official *liniment of soft soap* (p. 291).

The addition of glycerin during saponification is for the purpose of rendering the soap transparent. This is accomplished by preventing crystallization of the soap particles. Syrup or glucose may be used instead of glycerin as retarders.

The liquid soaps now so popular for toilet, surgical and shampoo use are prepared by saponifying cottonseed oil or coconut oil or mixtures of the two with potassium hydroxide.

While Castile soap, sodium stearate, and soft soap are the only official soaps, in the limited sense of the term, we have other official products, that are usually considered as soaps, although it is a question whether all of them are properly so grouped.

Linimentum Ammoniæ (N.F.), or *Volatile Liniment*, is made by shaking together 250 cc. of ammonia water, 10 cc. of oleic acid and 740 cc. of sesame oil. Whether it is a real soap or merely an emulsion of sesame oil in a small amount of ammonia soap can be figured out by molecular proportions, assuming as the reaction the following equation.

$$\begin{array}{ccccc} \text{Olein} & & \text{Ammonia water} & & \text{Ammonia liniment} \\ C_3H_5(C_{18}H_{33}O_2)_3 & + & 3NH_3 + 3H_2O & = & C_3H_5(OH)_3 + 3NH_4C_{18}H_{33}O_2. \\ 884 & & 51 & & \end{array}$$

This equation shows that every 884 Gm. of oil will require 51 Gm. of absolute ammonia (or 510 Gm. of 10 per cent ammonia water) for complete saponification. Comparison of these figures with the Formulary quantities will show that the amount of ammonia water there prescribed falls far short of this proportion.

Hartshorn liniment, as this preparation is popularly called, is a valuable and largely used embrocation.

Linimentum Calcis (N.P. X; N.F. VI), or *Lime Liniment*, is made mixing together 500 cc. of lime water and 500 cc. of linseed oil.

There is no question that this liniment is merely an emulsion of linseed oil in small amount of calcium-linseed oil soap. Calculations similar to those given under ammonia liniment, will show that the amount of calcium hydroxide is far short of the quantity required for complete saponification. The value of this liniment, popularly called *Carron oil*, in burns, has been mentioned on p. 523.

EMPLASTRUM PLUMBI OLEATIS—Lead Oleate Plaster

This preparation, the manufacture of which is described at length on page 609, is mentioned at this place as an example of a true soap, of that type which is insoluble in water. It is a lead oleopalmitate, even as soap U.S.P. is a sodium oleopalmitate.

The official *oleate of mercury* is scarcely to be considered as a soap, as it contains a large excess of oleic acid.

Ammonium Linoleate is now on the market and is recommended as an emulsifying agent in the preparation of toilet creams and similar products.

Sodium Ricinoleate is now recommended as a "detoxifying" agent in mouth infections and in the treatment of septicemias.

In many books on pharmacy the chapter on fats and soaps is considered the proper place to consider the petroleum products, but these have already been described on p. 639, for reasons mentioned there; hence at this place all that is necessary is the mention that animal and vegetable fats being the oleates, stearates, and palmitates of glyceryl, or closely allied bodies, when treated with sodium or potassium hydroxide, split into glycerin and soap; in other words, can be saponified. The mineral fats—petrolatum and similar products—do not saponify when treated with sodium or potassium hydroxide. Again, animal and vegetable fats, on standing, become oxidized, partially splitting into glycerin and the fatty acids, becoming rancid, as we say.

Petroleum fats do not turn rancid, do not oxidize, hence ointments made with vaselin and similar petroleum fats keep indefinitely. Petroleum, however, is not absorbed by the skin as readily as are the animal and vegetable fats.

WAXES

Among the derivatives of the fatty hydrocarbons higher than $C_{18}H_{38}$ some bodies of pharmaceutic interest are found. $C_{27}H_{56}$ yields ceryl alcohol or *cerotin* ($C_{27}H_{55}OH$), while the body, $C_{30}H_{61}OH$ or $C_{31}H_{63}OH$, is known as melissyl alcohol (sometimes called *myricyl alcohol*).

The ultimate analysis of these bodies containing a large number of carbon atoms does not enable us accurately to determine the formula. The difference in the percentage of carbon and hydrogen in the bodies $C_{30}H_{61}OH$ and $C_{31}H_{63}OH$ varies so slightly as to give rise to doubt as to which is the exact formula.

Thus, $C_{30}H_{61}OH$ has the molecular weight:

$C_{30} = 30 \times 12 = 360$
$H_{62} = 62 \times 1 = 62$
$O = 1 \times 16 = \underline{16}$

molecular weight, $\overline{438}$, and contains

Carbon, $\frac{360}{438} \times 100 = 82.19$ per cent.
Hydrogen, $\frac{62}{438} \times 100 = 14.15$ per cent.
Oxygen, $\frac{16}{438} \times 100 = 3.65$ per cent.
$\overline{99.99}$ per cent.

While $C_{31}H_{63}OH$ has the molecular weight:

$C_{30} = 31 \times 12 = 372$
$H_{64} = 64 \times 1 = 64$
$O = 1 \times 16 = \underline{16}$

molecular weight, $\overline{452}$, and contains

Carbon, $\frac{372}{452} \times 100 = 82.30$ per cent.
Hydrogen, $\frac{64}{452} \times 100 = 14.15$ per cent.
Oxygen, $\frac{16}{452} \times 100 = 3.54$ per cent.
$\overline{99.99}$ per cent.

The difference in percentage of carbon in these substances (82.19 per cent and 82.30 per cent) is no greater than the permissible limit of error in analysis; while the percentage of hydrogen in the two is identical.

The oxidation of ceryl alcohol yields *cerotic acid*, $C_{26}H_{53}COOH$, while the oxidation of melissyl alcohol gives *melissic acid*, $C_{23}H_{59}COOH$ or $C_{30}H_{61}COOH$.

These bodies are of interest as constituents of the various waxes, they being esters of the two alcohols, with the two acids just mentioned and other fatty acids.

CERA FLAVA—Yellow Wax

(Cera Flav.—Beeswax)

Yellow Wax is the purified honeycomb of the bee, *Apis mellifera* Linné (Fam. *Apidæ*).

Summarized Description.

Yellow to gray-brown solid; agreeable honey-like odor; faint characteristic taste; brittle in the cold; plastic at heat of the hand; insoluble in water; sparingly soluble in cold alcohol; partly soluble in hot alcohol; completely soluble in chloroform, ether and in fixed and volatile oils; sp. gr. 0.950 to 0.960; melts between 62° and 65° C. For details, see U.S.P., p. 114.

For *tests for identity*, for *impurities* (fats, fatty acids, Japan wax, rosin, carnauba wax, soap), see U.S.P., p. 114.

Ester Number.—72 to 77. Details, see U.S.P.

Acid Number.—18 to 24. Details, see U.S.P.

Composition.—The official beeswax consists chiefly of melissyl palmitate, $C_{30}H_{61}C_{16}H_{31}O_2$, melissyl melissate, $C_{30}H_{61}C_{30}H_{59}O_2$, and free cerotinic acid.

Gascard and Damoy by refined methods of separation have recently isolated from beeswax, 4 hydrocarbons, 4 alcohols and 4 acids. Of these, the important constituents are ceryl and melissyl alcohols and cerotic and melissic acids.

Remarks.—Yellow wax is defined as a concrete substance prepared by *Apis mellifera*, and is a well-known commercial product, consisting of the comb the bee prepared in which to store its honey, and is an excretion of the animal itself.

In obtaining wax the comb is taken, drained of its honey, washed in cold water, and then melted and strained, the product being a yellow solid, of pleasant, aromatic odor, having specific gravity 0.950 to 0.960, melting at 62° to 65° C.

The large demand for wax has led to many adulterations of same, the favorite sophistication being rosin or paraffin. For detecting these, neither the specific gravity nor the melting point is a criterion of quality, for although paraffin has a lower specific gravity than that of wax, and rosin a higher specific gravity, a combination of the two can be made to possess the same specific gravity as pure wax; hence chemical tests of the Pharmacopœia are essential for intelligent examination. The test for rosin is that when a sample is boiled with 15 per cent solution of soda and filtered, such filtrate should give no precipitation on addition of acid.

In other words, wax itself is unaffected by 15 per cent sodium hydroxide, whereas the rosin dissolves, forming potassium abietinate. Therefore, if rosin is present, the filtrate contains this potassium abietinate, and the solution when treated with acid precipitates the free abietinic acid.

If the alkaline solution is filtered through paper it will dissolve some of the paper pulp, which will be precipitated on addition of acid, leading to wrong conclusions; hence the present Pharmacopœia directs filtration through asbestos.

A useful test for paraffin is based on the fact that wax is decomposed by boiling with sulfuric acid, while paraffin remains unchanged, as explained under Paraffin. This test is not given in the monograph of the present Pharmacopœia; the absence of paraffin being determined by the ester number (see p. 1022). Pure wax has an ester number of from 72 to 77, while paraffin is 0,· and admixtures run somewhere between 0 and 72.

CERA ALBA—White Wax

(Cer. Alb.—Bleached Beeswax)

Yellow Wax, bleached.

Summarized Description.

Yellowish-white somewhat translucent solid; faint characteristic odor; nearly tasteless; free from rancidity; sp. gr. 0.950 to 0.960; melts between 62° and 65° C. For details, see U.S.P., p. 113.

For *test for identity* and for *impurities*, see Cera Flava.

Ester Number.—72 to 77. See Part V.

Acid Value.—18 to 24. See Part V.

Remarks.—White wax represents the yellow variety which has been bleached by exposing to sunlight in thin layers. Chemical methods of bleaching are sometimes employed, but the product is not as good as is the sun-bleached. Much of the white wax of commerce is adulterated with paraffin.

CETACEUM—Spermaceti

(Cetac.)

A waxy substance obtained from the head of the sperm whale, *Physcter macrocephalus* Linné (Fam. *Physeteridæ*).

Summarized Description.

White, somewhat translucent, slightly unctuous masses; scaly crystalline fracture; pearly luster; bland mild taste; insoluble in water; almost insoluble in cold alcohol; soluble in boiling alcohol, ether, chloroform, carbon disulfide, fixed and volatile oils; sp. gr. 0.938 to 0.944; melts between 42° and 50° C. For details, see U.S.P., p. 116.

For *tests for identity*, for *impurities* (paraffin, stearic acid), see U.S.P., p. 116.

Remarks.—Spermaceti is obtained from the whale by removing from the recently killed animal the oily liquid contained in a cavity in the head. This oil soon congeals and is then submitted to strong pressure. After the liquid part has been expressed, the press cake, crude spermaceti, is purified by melting in water, then boiling with weak alkali, and then washing with water.

Spermaceti consists chiefly of cetyl palmitate, $C_{16}H_{33}C_{16}H_{31}O_2$ (p. 725), and is a white, somewhat translucent solid, breaking with a scaly fracture, having a specific gravity of 0.938 to 0.944, melting at between 42° and 50° C. It is a constituent of cold cream, and its chief use is for hardening ointments.

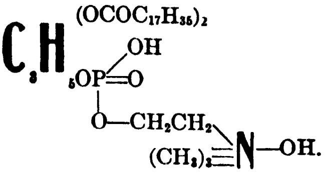
Cetyl Alcohol obtained by treatment of spermaceti with alkali under proper conditions, serves as an admirable water-absorbing ointment base.

Chinese Wax is chiefly ceryl cerotate, $C_{27}H_{55}C_{27}H_{53}O_2$, and is the secretion from an insect living on the tree *Ligustrum lucidum.* It is frequently confounded with *Japanese wax,* which is of vegetable origin, being found in the fruit of *Rhus succedanea.*

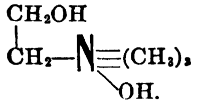
LECITHIN AND THE STEROLS

These substances can best be discussed at this place, since they are allies of fats.

Lecithin is a complex ester of glycerin having the graphic formula



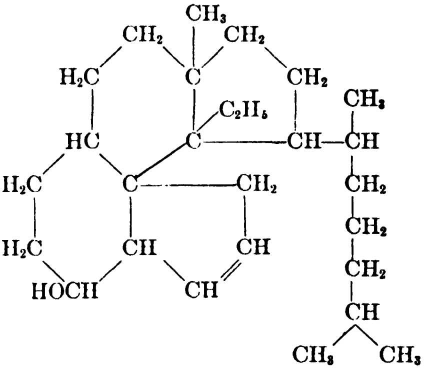
On analyzing this formula, we find that the glyceryl group is combined with two stearic acid groups, and a phosphoric acid group; while to the latter is attached a choline group,



Barbieri and others claim that it is not a definite chemical but a mixture of olein, stearin, a substance containing nitrogen, sulfur and phosphorus, called "ovine," and cholesterol.

The sterols are monohydric alcohols whose constitution includes both six- and five-membered carbon rings. Flesh foods contain cholesterols; plant foods contain phytosterols.

Cholesterol, $C_{27}H_{45}OH$, is the alcohol constituent of the main ester of wool fat (p. 739). Its graphic formula is supposed to be:



Lecithin and Cholesterol are found in the brain, yolk of egg and ox-gall (p. 966).

Rosenheim and others indicate that cholesterol is allied structurally with the bile acids (p. 966).

Isocholesterol is an isomere of cholesterol, found in wool fat (p. 739).

Ergosterol, $C_{28}H_{44}O$ or $C_{29}H_{46}O$, is a phytosterol first obtained from ergot. It is now obtained commercially from yeast. Irradiated ergosterol and also, to a lesser extent, irradiated cholesterol are found to act like Vitamin D (p. 957).

BIBLIOGRAPHY

Heptane.—Kremers, Jl. A.Ph.A., 7, 1918, 343; 9, 1920, 857, 860 and 1153; 10, 1921, 26; Hill, Science Supp., 72, Sept. 26, 1930, xiv.

Ethyl Oenanthate.—Rogers, Jl. A.Ph.A., 12, 1923, 503.

Nonane.—Clark and Adams, Ch. News, 114, 1916, 3.

Nonyl Aldehyde.—Parry, Ch. and Dr., 77, 1910, 531.

Duodecyl Aldehyde.—Umney, C.A., 6, 1912, 793.

***Stearic Acid.*—(Structure) Grün, B., 39, 1906, 4400. (Manufacture) Olive, Jl. Soc. Ch. Ind., 49, 1930, 153B; Cranor, Jl. Ind. Eng. Ch., 21, 1929, 719. (Standards) Anon., C.A., 22, 1918, 1245. (Uses) Dismore, Jl. Ind. Eng. Ch., 21, 1929, 722.**

Margaric Acid.—Wanklyn and Johnstone, Ch. and Dr., 39, 1891, 745; Ruttan, 8th Int. Cong. App. Ch., 25, 1912, 431; Thomson, C.A., 22, 1928, 1326; Shriner and co-workers, Jl. Am. Ch. Soc., 55, 1933, 1499.

Oleic Acid.—(History) Beringer, A.J.P., 83, 1911, 213. (Structure) Harries, B., 39, 1906, 3728; Fahrion, C.A., 10, 1916, 1278. (Manufacture) Saunders, N.R., 9, 1880, 162.

Elaidic Acid.—(Structure) Lewkowitsch, 1, 1909, 148. (Elaidin reaction) Braconnot, Jl. de Ph. 1, 1815, 393.

Linoleic Acid.—(Structure) Goldsobel, Ch. Zt., 30, 1906, 825; Takahashi, C.A., 15, 1921, 2273; Armstrong and Allen, Jl. Soc. Ch. Ind., 43, 1924, 207.

Ricinoleic Acid.—(Structure) Walden and Krafft, B., 27, 1894, 3471; Goldsobel, *ibid.*, 27, 1894, 3121; Thoms and Deckert, Ph. Ztg., 65, 1920, 753; Stosius and Wiesler, C.A., 15, 1921, 1298. (Manufacture) Tokin, C.A., 5, 1911, 3923.

Petroselinic Acid.—Vongerichten and Koehler, B., 42, 1909, 1638.

Juniperic Acid.—Bougault, Jl. de Ph., [7], 1, 1910, 425.

Behenic Acid.—Walter, A.J.P., 19, 1847, 78.

Chaulmoogric Acid.—Hirschfelder, Jl. Ind. Eng. Ch. 15, 1923, 457.

Polysolve and Oleite.—Jacobs, Am. Dr., 18, 1884, 22; Kilmer, A.Ph.A., 37, 1889, 210.

Hydrogenated Oils.—(Manufacture) Ellis, 31, 1912, 1155; Frerichs, Arch. d. Pharm., 253, 1915, 512; Lush, Jl. Soc. Ch. Ind., 42, 1923, 2197; Normann, Jl. Soc. Ch. Ind., 41, 1922, 469R; Sadtler, A.J.P., 95, 1923, 281; Sabatier, Jl. Soc. Ch. Ind., 46, 1927, 682; Ed., *ibid.*, 46, 1927, 571; Bolton, *ibid.*, 46, 1927, 444T; Armstrong, *ibid.*, 50, 1931, 968 and 51, 1932, 92; Phillips, 52, 1933, 51. (Properties) Mannich and Thiele, Dr. Circ., 62, 1918, 75; Wesson, C.A., 14, 1920, 2723. (Uses) Linnett, Pract. Dr. 35, Feb., 1917, 34; Kyser and Mayo, Jl. A.Ph.A., 8, 1919, 816; Fiero, Jl. A.Ph.A., 20, 1931, 254.

Intarvin.—McKee, Jl. Ind. Eng. Ch. (News Ed.), 1, 1923, 1; Keefer and co-workers, C.A., 19, 1925, 1002.

Sajodin.—Fischer and von Mering, Ch. Cent., 77^1, 1906, 953; Germ. Pat. No. 180,087, *ibid.*, 78^1, 1907, 434; Germ. Pat. 186,214, *ibid.*, 78^1, 1907, 956.

Oils and Fats.—(Extraction) Brewis, Jl. Soc. Ch. Ind., 43, 1924, 111; Amery, Jl. Soc. Ch. Ind., 49, 1930, 300. (Composition) Armstrong and Allen, Jl. Soc. Ch. Ind., 43, 1924, 207T; Hilditch, *ibid.*, 49, 1930, 210. (Refining) Andrews, *ibid.*, 46, 1926, 970; (Classification) Rosenbloom and Gies, C.A., 6, 1912; Allen, 2^1, 1901, 87. (Rancidity) Powick, Jl. Soc. Ch. Ind., 43, 1924, 302B; Tschirch and Barben, C.A., 18, 1924, 2970; Husa, Jl. A.Ph.A., 15, 1926, 1071; 17, 1928, 243 and 19, 1930, 825; Fiero, A.J.P., 102, 1930, 146; Vilbrand, C.A., 25, 1931, 4426.

Olive Oil.—(History) Hurley, Pract. Dr., 36, Aug., 1918, 22; Sept., 1918, 21; Oct., 1918, 21 and Nov., 1918, 22. (Production) Rousseau, Jl. Soc. Ch. Ind., 45, 1926, 953B; Traetta, *ibid.*, 45, 1926, 677B; Hommell, Pract. Dr., 47, Feb., 1929, 19; Musher, C.A., 23, 1929, 2053. (Composition) Hehner and Mitchell, Analyst, 21, 1896, 328; Jamieson and Baughman, Jl. Frank. Inst., 200, 1925, 131; Jamieson, C.A., 22, 1928, 691; Täufel and Sarria, Jl. Soc. Ch. Ind., 45, 1926, 332B. (Properties) Hommell, see above; Deuble and Schoetzow, Jl. A.Ph.A., 20, 1931, 655. (Adulterants) LaWall, A.J.P., 100, 1928, 616. (Tests) Becchi, A.Ph.A., 35, 1887, 281; Meyer, A.J.P., 73, 1901, 560; Sage, Ph. Jl., 94, 1915, 128 and 193. (Antiseptic properties) Hill and Macht, C.A., 17, 1923, 3521.

Sesame Oil.—(History and properties) Raubenheimer, A.J.P., 82, 1910, 476. (Constituents) Farnsteiner, through Lewkowitsch, 2, 1909, 175; Lane, Jl. Soc. Ch. Ind., 20, 1901, 1083; Jamieson and Baughman, Jl. Am. Ch. Soc., 46, 1924, 778; Adriani, C.A., 23, 1929, 2054, Better, C.A., 25, 1931, 5782. (Tests) Vellavechia and Fabres, Jl. Soc. Ch. Ind., 13, 1894, 69; Cook, Jl. A.Ph.A., 19, 1930, 361.

Cottonseed Oil.—(Composition) Matthes and Heinz, Arch. d. Pharm., 247, 1909, 161; Jamieson and Baughman, Jl. Am. Ch. Soc., 42, 1920, 1197; Anderson and Moore, *ibid.*, 45, 1923, 1944. (Tests) Ivanov, Jl. Soc. Ch. Ind., 47, 1928, 236B.

Linseed Oil.—(Constitution) Hazura, A.Ph.A., 59, 1887, 618; Fahrion, Zt. angew. Ch., 23, 1910, 722 and 1106; Ellis, Jl. Soc. Ch. Ind., 44, 1925, 401T, 463T, 469T, 486T and 45, 1926, 193T; Eibner and Brosel, C.A., 22, 1928, 4852; Theis and co-workers, Jl. Ind. Eng. Ch., 21, 1929, 1244; Haworth, C.A., 23, 1929, 4671; Gay, Jl. Soc. Ch. Ind., 51, 1932, 126T; Bauer and Hazura, Jl. Soc. Ch. Ind., 7, 1888, 680; Erdmann, B., 42, 1909, 1324 and 1334 and Zt. physiol. Ch., 74, 1911, 179; Rollett, Zt. physiol. Ch., 62, 1909, 410. (Properties) Niegermann and Kayser, C.A., 8, 1914, 2496; Muehler, *ibid.*, 8, 1914, 2496; Fahrion, C.A., 14, 1920, 2556; ("Driers") Rasquin, C.A., 19, 1927, 3601; Chase, C.A., 26, 1932, 3389.

Castor Oil.—(History) Evers, Ph. Jl., 129, 1932, 372. (Composition) Khonovski, C.A., 6, 1912, 737. (Production) Shrader, Jl. Soc. Ch. Ind., 39, 1920, 392R. (Properties) Pereira, Ph. Jl., 9, 1850, 499; May, Spatula, 16, 1909, 22; Overlach, A.Ph.A., 57, 1909, 360; Langton, Jl. Soc. Ch. Ind., 50, 1931, 213T. (Pharmacology) Chistoni, C.A., 14, 1920, 2823.

Sodium Ricinoleate.—Larson and Nelson, Pract. Dr., 47, Sept., 1929, 33; Miller and Castles, C.A., 26, 1932, 2211.

Croton Oil.—(Composition) Schmitt and Behrendes, A.Ph.A., 26, 1878, 501; Kobert, Ph. Jl., [3], 20, 1890, 978; Boehm, Arch. Pharm., 253, 1915, 574 and Ph. Zt., 61, 1916, 116. (Tests) Anon, Ph. Jl., 97, 1916, 137.

Chaulmoogra Oil.—(Production) Anon., Pharm. Era, 54, 1921, 129; Rock, Jl. A.Ph.A., 10, 1921, 631; Muir, C.A., 19, 1925, 872; Power, Jl. A.O.A.C., 8, 1925, 525. (Composition) Power, Jl. Ch. Soc., 85, 1904, 629 and 838; 87, 1905, 895; 91, 1907, 557; 93, 1908, 252; A.J.P., 87, 1915, 493; Hashimoto, Jl. Am. Ch. Soc., 47, 1925, 2325; Wrenshall and co-workers, C.A., 19, 1925, 2476; Shriner and Adams, C.A., 20, 1926, 172; Peacock and Aiyar, Jl. Soc. Ch. Ind., 50, 1931, 552B; Buckley and Teik, *ibid.*, 51, 1932, 391B. (Pharmacology) Dean and co-workers, Dr. Circ., 63, 1919, 504; *ibid.*, 64, 1920, 426; Jl. Am. Ch. Soc., 42, 1920, 2626; Anon., Jl. A.M.A., 75, 1920, 1361; McDonald, Jl. A.M.A., 75, 1920, 1071; Walker and Sweeny, C.A., 14, 1920, 1580; Warren, Jl. A.Ph.A., 10, 1921, 511; Schobl and co-workers, Jl. Soc. Ch. Ind., 43, 1924, 765B and 995B; Perkins, C.A., 20, 1926, 1275; Wayson, C.A., 24, 1930, 890.

Chaulmoogra Esters.—Dean and Wrenshall, Jl. Am. Ch. Soc., 42, 1920, 2626; Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 457; Adams and co-workers, Jl. Am. Ch. Soc., 51, 1929, 1261.

Coconut Oil.—Boemer and Baumann, Ph. Cent., 61, 1920, 727; Blokzeyl, Pharm. Era, 57, 1923, 609; Armstrong and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 63T; Taylor and Clark, Jl. Am. Ch. Soc., 49, 1927, 2829; Collin and Hilditch, Jl. Soc. Ch. Ind., 47, 1928, 291T; Williams, C.A., 25, 1931, 4633.

Corn Oil.—(Production) Sievers, C.A., 15, 1921, 953; Jamieson, Jl. Am. Ch. Soc., 43, 1921, 2696 and 45, 1923, 1090. (Composition) Anderson and Shriner, Jl. Am. Ch. Soc., 48, 1926, 2976. (Tests) Thurston, Mid. Dr., 52, 1918, 155.

Peanut Oil.—(Composition) Heiduschka and Felser, Jl. Soc. Ch. Ind., 39, 1920, 272A; Jamieson and co-workers, Jl. Am. Ch. Soc., 43, 1921, 1372. (Properties) Raubenheimer, Proc. N.J.Ph.A., 48, 1918, 69.

Tung Oil.—Rhodes and Ling, Jl. Ind. Eng. Ch., 16, 1924, 1051; Toch, Jl. Soc. Ch. Ind., 45, 1926, 199B; Stegen and Van Loon, *ibid.*, 47, 1928, 361T; Boeseken, *ibid.*, 48, 1929, 71T; Jordan, *ibid.*, 48, 1929, 847; Morrell and Marks, *ibid.*, 50, 1931, 549B; Foote, Jl. A.Ph.A., 20, 1931, 295; Gardner, Jl. Ind., Eng. Ch., 24, 1932, 687.

Soy Bean Oil.—(History) Horvath, Jl. Ind. Eng. Ch., News Ed., 9, May 10, 1931, 136. (Composition) Lewkowitsch, C.A., 5, 1911, 597; Low, Jl. Ind. Eng. Ch., 12, 1920, 572; Baughman and Jamieson, Jl. Am. Ch. Soc., 44, 1922, 2947; Pfahler, Jl. Soc. Ch. Ind., 45, 1926, 413B; Heiduschka and Eger, *ibid.*, 50, 1931, 727B. (Properties) Howell, Jl. A.Ph.A., 7, 1918, 159; Laucks and Banks, C.A., 14, 1920, 2271; Adolph and Kiang, *ibid.*, 14, 1920, 2518.

Palm Oil.—Bomer and Schneider, C.A., 18, 1924, 2081; Armstrong and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 143; Drummond, *ibid.*, 45, 1926, 994; Langton, *ibid.*, 47, 1928, 655; Hilditch and co-workers, *ibid.*, 47, 1928, 281; 48, 1929 and 49, 1930, 363T.

Oil of Theobroma.—(Composition) Traub, A.Ph.A., 31, 1883, 239; Mattes and Pohdech, A.Ph.A., 57, 1909, 351; Morgan and Bowen, Jl. Soc. Ch. Ind., 43, 1924, 346T; Lea, *ibid.*, 48, 1929, 41T; Bougault and Schuster, C.A., 25, 1931, 3856; Labbé and co-workers, C.A., 25, 1931, 729. (Properties) Horn and Osol, A.J.P., 101, 1929, 601. (Uses) Duhamel, A.J.P., 13, 1832, 18.

Cod Liver Oil.—(History and manufacture) Munn, Montreal Ph. Jl., 25, 1914, 192; Drummond and Zilva, Jl. Soc. Ch. Ind., 41, 1922, 280T; *ibid.*, 42, 1923, 167T; Langton, Jl. Soc. Ch. Ind., 47, 1928, 1337; Bills, Ch. Rev., 3, 1927, 848; Davies, Pract. Dr., 50, Nov., 1932, 19; England, A.J.P., 23, 1929, 3305. (Composition) Pereira, Ph. Jl. 8, 1849, 370; Gauthier and Mourges, Jl. de Ph. et Ch., 31, 1890, 2532; Chapman, Ph. Jl., 97, 1916, 571; Mastbaum, *ibid.*, 96, 1916, 327; Heilbron, Jl. Soc. Ch. Ind., 45, 1926, 181. (Properties) Apple, Apoth., 22, 1910, 22. (Medical action) Parke and Howland, Jl. A.M.A., 77, 1921, 2122; Fantus, Jl. A.Ph.A., 14, 1925, 592. (Tests) Fuller, Dr. Circ., 58, 1915, 569. (Gaduol, etc.) Chapoteaut, Am. Dr., 15, 1886, 36. (Uses) Williams, Ph. Jl., 89, 1912, 806; Shabad and Sorochovich, C.A., 7, 1913, 818. (Vitamins of) Drummond and co-workers, Jl. Soc Ch. Ind., 43, 1924, 236T; Holmes, Jl. Ind. Eng. Ch., 16, 1924, 295, 964 and 1181; Pract. Dr., 44, Apr., 1926, 20; Dubin and Funk, C.A., 19, 1925, 1726.

Sodium Morrhuate.—Rogers, Ph. Jl., 103, 1919, 434; Biesenthal, C.A., 15, 1921, 1160; Berghausen and Stenkoenig, A.J.P., 93, 1921, 757.

Halibut Liver Oil.—Emmett and Bird, Jl. Ind. Eng. Ch., 24, 1932, 1073; Anon., Dr. Circ., 76, Feb., 1932, 30.

Lard.—(Composition) Lewkowitsch, 2, 1909, 570. Twitchell, Jl. Am. Ch. Soc., 17, 1895, 294; Hurd and co-workers, Jl. Am. Ch. Soc., 52, 1930, 1135. (Preservation) Eberle, A.J.P., 39, 1867, 349; Doliber, A.Ph.A., 15, 1867, 385; Van Noren, Nat. Dr., 40, 1910, 78.

Wool Fat.—(History) Rice, Am. Dr., 15, 1886, 44, 62, 77, 90, 98 and 108; Hallberg, A.Ph.A., 37, 1889, 96. (Manufacture) Langbeck, Jl. Soc. Ch. Ind., 9, 1890, 356; Salisbury, Pharm. Era, 50, 1917, 279; Anon., Ph. Week, 54, 1917, 376; Dubosc, C.A., 14, 1920, 1615; Stocking, Ph. Era, 62, Feb. 27, 1926, 7. (Composition) De Sanctis, A.Ph.A., 42, 1894, 638; Marchetti, A.Ph.A., 44, 1896, 774; Lewkowitsch, Jl. Soc. Ch. Ind., 11, 1892, 135 and 15, 1896, 14; Drummond and Baker, Jl. Soc. Ch. Ind., 48, 1929, 232T; Windaus and Tschesche, C.A., 24, 1930, 5042; Salamone, C.A., 25, 1931, 2314. (Test) Windaus, Arch. d. Pharm., 246, 1908, 123.

Eucerin.—Unna, Dr. Circ., 56, 1912, 399; Roemer, Dr. Circ., 57, 1913, 36; Lifschütz, C.A., 24, 1930, 686.

Sweet Almond.—(Constituents) Boullay, Jl. de Ph., 3, 1817, 342, Bul., A.J.P., 21, 1849, 354; Portes, Jl. de Ph. et Ch., 25, 1877, 30; Ludwig, Arch. d. Pharm., 199, 1872, 420; Rosenthaler and Seiler, Sch. Ap. Zt., 60, 1922, 522; Hart-Pitman, Jl. Ind. Eng. Ch., 22, 1930, 1128 and 1129.

Flaxseed.—(Constituents) Beringer, A.J.P., 59, 1887, 286; Kirchner and Tollens, A., 175, 1875, 216; Helger, B., 36, 1903, 3197; Jorissen and Hairs, Jl. de Ph. et Ch., 24, 1891, 259; Neville, A.Ph.A., 59, 1911, 226 and C.A., 7, 1913, 2445; Van Kampen, C.A., 8, 1914, 1473; Anderson and Crowder, Jl. Am. Ch. Soc., 52, 1930, 3711. (Test for starch) Lloyd, A.Ph.A., 43, 1895, 196.

Pumpkin Seed.—(Constituents) Power and Salway, Jl. Am. Chem. Soc., 32, 1910, 346. (Pharmacology) Sollmann, Jl. A.M.A., 72 (1919) 1228; Neely and Davy, Jl. A.Ph.A., 20, 1931, 555; Rath, C.A., 25, 1931, 4057.

Watermelon Seed.—Althausen and Kerr, Ph. Jl., 127, 1931, 50.

Lycopodium.—(Collection) Muszynski, Ph. Jl., 110, 1923, 64 and Jl. Soc. Ch. Ind., 51, 1932, 287B. (Constituents) Rathje, Arch. Pharm., 246, 1908, 699; Zetzsche and Huggler, C.A., 22, 1928, 2949; Bauer and Piners, Jl. Soc. Ch. Ind., 49, 1930, 247B.

Castor Beans.—(Constituents) Krausz, C.A., 5, 1911, 2495; Jalander, *ibid.*, 6, 1912, 635; Winterstein, Keller and Weinhagen, Arch. Pharm., 255, 1917, 513; Jl. ph. ch., 22, 1920, 147; Böttger, B., 51, 1918, 673; Spaeth and Tschelnitz, Dr. Circ., 69, 1925, 26. (Toxicity) Dowzard, Jl. A.Ph.A., 12, 1923, 116.

Soap.—(History) Anon., Nat. Dr., 40, 1910, 411; Abraham, Jl. A.Ph.A., 5, 1916, 295; Anon., Ch. and Dr., 90, 1918, 589; Penny, Jl. Soc. Ch. Ind., 47, 1928, 258; Bailey, N. Y. Jl. Ph., 10, 1933, 119. (Composition) Richardson, Jl. Am. Ch. Soc., 30, 1908, 414; Leimdörfer, C.A., 6, 1912, 1378; Lewkowitsch, 3, 1909, 273. (Manufacture) Anon., Am. Dr., 15, 1886, 181; Pennock, Jl. Am. Ch. Soc., 28, 1906, 1242; Thum, A.J.P., 83, 1911, 111; Smith, Ph. Jl., 95, 1915, 33; Wolff, C.A., 14, 1920, 1904; Clark, C.A., 22, 1928, 2851; Schuck, C.A., 23, 1929, 5342; Smith, Jl. Soc. Ch. Ind., 51, 1932, 337T. (Properties) Leimdoerfer, C.A., 14, 1920, 1454.

Castile Soap.—Lockwood, Dr. Circ., 64, 1920, 91.

Soft Soap.—Raubenheimer, Pharm. Era, 44, 1911, 26.

Liquid Soap.—Jones, Dr. Circ., 58, 1914, 728.

Ceryl Alcohol.—Gascard, Jl. Soc. Ch. Ind., 39, 1920, 495A.

Myricyl Alcohol.—Heiduschka and Gareis, C.A., 14, 1920, 935; Gascard, Jl. ph. ch., 22, 1920, 935.

Wax.—(Origin) Maeterlinck, Life of the Bee. (Composition) Schwalb, A., 235, 1886, 148; Damoy, Compt. rend., 177, 1923, 1222 and 1442; Jl. ph. ch., 29, 1924, 148 and 225. (Properties) Deeney, A.J.P., 104, 1932, 19. (Tests) Arny, A.J.P., 72, 1900, 74. (Bibliography) Anon., Jl. Soc. Ch. Ind., 11, 1892, 756.

White Wax.—(Preparation) Babcock, A.Ph.A., 15, 1867, 372; Ramboe, Jl. Soc. Ch. Ind., 16, 1897, 150; Nicolai, C.A., 24, 1930, 1533.

Spermaceti.—(Preparation) Tschirch, Handbuch, 1912, 742. (Composition) Heintz, A., 92, 1854, 299. (Specific gravity) Lundin, Ph. Week., 53, 1916, 1000.

Cetyl Alcohol.—Richter, Ph. Jl., 127, 1931, 321.

Chinese Wax.—Kebler, Am. Dr., 27, 1895, 4.

Japanese Wax.—Kühl, Ap. Zt., 22, 1907, 1137.

Lecithin.—Barbieri, Comp. rend., 145, 1907, 133; Riedel, C.A., 7, 1913, 802; Brün and Limpächer, C.A., 18, 1924, 536; Rewald, C.A., 22, 1928, 3178; Sonol, C.A., 23, 1929, 237; Sibbald, Jl. Soc. Ch. Ind., 52, 1933, 175.

Cholesterol.—Windaus, Arch. d. Pharm., 246, 1908, 123; B., 41, 1908, 2558; 42, 1909, 3770; 47, 1914, 1229; 48, 1915, 1064; 52B, 1919, 162; 53B, 1920, 488 and 614; 54B, 1921, 1059; C.A., 14, 1920, 3649; C.A., 17, 1923, 1434; Levene, Jl. Am. Ch. Soc., 39, 1917, 828; Wieland, Zt. physiol. Ch., 140, 1924, 186; *ibid.*, 161, 1926, 80; *ibid.*, 167, 1927, 70; Drummond, Jl. Soc. Ch. Ind., 45, 1926, 997; Cuny, Jl. ph. et ch., 8, 1928, 62; De Fazi and co-workers, C.A., 26, 1932, 149, 991 and 4058; Pirrone, C.A., 26, 1932, 4341; Montignie, C.A., 23, 1929, 2446; Hummel, C.A., 24, 1930, 1147; Rosenheim and King, Jl. Soc. Ch. Ind., 51, 1932, 464 and 954; Tschesch, A., 498, 1932, 185; Schoenheimer, Science, 74, 1931, 582.

Phytosterols.—Klobb, C.A., 6, 1912, 610.

Ergosterol.—Hess and Lewis, Jl. A.M.A., 91, 1928, 783; Windaus, C.A., 24, 1930, 4518; Montignie, C.A., 23, 1929, 858; De Boe, C.A., 25, 1931, 1836; Hart and coworkers, Jl. A.C.S., 52, 1930, 2013, 2015, 2017, 3688; *ibid.*, 54, 1932, 1074; Schoenheimer, Science, 74, 1931, 581; Heilbron and Simpson, Jl. Ch. Soc., 1932, 2400; Bills, U. S. Pat. 1,842,929, Jan., 1932; Heilbron, Jl. Ch. Soc., 51, 1932, 1063.

CHAPTER XLII

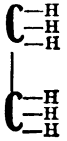
ORGANIC PRODUCTS OF INTERMEDIATE CHARACTER

Among the organic chemicals used in pharmacy are several which can scarcely be grouped either as derivatives of hydrocarbons of the fatty series or of the aromatic series. Among these bodies are classed the cyanogen bodies, carbonic acid derivatives, and a few ringed bodies of character midway between the aliphatic compounds already described and the aromatic bodies.

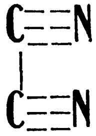
CYANOGEN BODIES

The cyanides can be considered as ethyl or methyl derivatives in which some of the hydrogen is replaced by nitrogen, as can best be shown by comparison of the formulas of ethane and cyanogen.

Ethane.



Cyanogen.

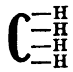


Cyanogen, $(CN)_2$, was discovered by Gay-Lussac in 1815, and is made by heating silver cyanide. It is a gaseous body of such poisonous characteristics as to render its manufacture and use unsafe.

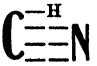
A derivative of same, however, paracyanogen, $(C_2N_2)_3$, is of interest in pharmacy, as the black precipitate which forms in hydrocyanic acid solution on standing.

Hydrocyanic Acid (HCN).—This substance was isolated by Scheele in 1782 from oil of bitter almond, and can be considered as methane, in which three of the hydrogen atoms are replaced by one of nitrogen, as shown by comparison of formulas given below:

Methane.



Hydrocyanic acid.



According to Dadieu, and also Enklaar, ordinary hydrocyanic acid consists of a mixture of the isomeres H—C≡N and H—N≡C (see p. 793).

As mentioned above, it is one of the products found in volatile oil of almond, and a description of the process whereby it is extracted will be left until this official is reached. (See p. 793.)

It is prepared by either of the processes given under diluted hydrocyanic acid, or by treating chloroform with ammonia gas under pressure, viz.,

$$CHCl_3 + NH_3 = HCN + 3HCl.$$

Pure hydrocyanic acid is a very poisonous gas, soluble in water, and used in medicine only in dilute form.

Acidum Hydrocyanicum Dilutum (U.S.P. IX; N.F. VI), or *diluted hydrocyanic acid*, is an aqueous solution containing about 2 per cent of hydrocyanic acid gas. It is prepared by distilling a mixture of potassium ferrocyanide with sulfuric acid and water, in a retort, and diluting distillate until it is 2 per cent strength.

For a simple extemporaneous method of preparing the diluted acid, however, the last Pharmacopœia directed the treating of silver cyanide with hydrochloric acid and a sufficient quantity of distilled water, the advantage of this process being that it does not require distilling, the silver cyanide combining with the hydrochloric acid and forming insoluble silver chloride, while the hydrocyanic acid goes into solution.

Dilute hydrocyanic acid is a colorless liquid, which is not very stable, and should be dispensed only when comparatively fresh; hence it is advantageous to manufacture same from silver cyanide. A trace of hydrochloric acid (acting as a retarding catalyst) preserves diluted hydrocyanic acid.

It possesses a pungent odor (characteristic of bitter almond oil or peach kernel), and should be both smelled and tasted with utmost caution, even in the dilute form. It is used as a sedative and expectorant.

Dose.—0.1 cc. (1½ minims).

Antidotes.—Sodium nitrite plus sodium thiosulfate; sodium nitrite alone; methylene blue; sodium thiosulfate. Relative efficacy in the sequence just given.

Mention should be made of the fact that formerly *Scheele's hydrocyanic acid* was a popular form of administering this chemical. It contained 5 per cent absolute hydrocyanic acid, and the confusion arising from the use of these two strengths of the acid (5 per cent and 2 per cent) was positively dangerous. At present, however, Scheele's acid is very rarely employed.

Hydrocyanic acid forms salts with metals, such products being called cyanides. There are no metallic cyanides recognized in U.S.P. X, although former Pharmacopœias recognized potassium cyanide (p. 473) and sodium cyanide (p. 495).

Hydrocyanic acid also forms ester-like compounds with organic radicals. As an example might be cited methyl cyanide, CH_3CN. The term cyanide, however, is not applied to these bodies, they being called *nitriles*, and in these bodies the radical is directly attached to the carbon atom and not to the nitrogen. In this way they differ from the *isonitriles*, which are isomeric bodies in which the radical is attached to the nitrogen instead of the carbon. The difference between these bodies is best shown by the appended graphic formulas:

Methyl nitrile.	Methyl isonitrile.
$CH_3—C\equiv N$	$CH_3—N\equiv C$

Isonitriles are of interest only as being exceedingly poisonous gases of disgusting odor, such as phenyl isonitrile, which is formed in a test for chloroform. (See p. 646.)

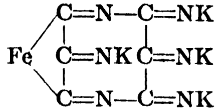
Cyanogen forms compounds with iron, forming ferrocyanides and ferricyanides, according to the valence of the metal. One of these (potassium ferrocyanide) was official in U.S.P. VIII; while each is recognized by U.S.P. XI as a test solution. The former of these bodies has been discussed among the potassium compounds, but this is the proper place for chemical comparison of these two interesting substances.

Potassium Ferrocyanide, $K_4Fe(CN)_6$, may be considered, for the sake of remembering the formula, as a combination of one molecule of ferrous cyanide, $Fe(CN)_2$, with four molecules of potassium cyanide; that is, $Fe(CN)_2 + 4KCN$.

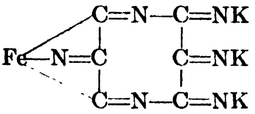
Potassium Ferricyanide can be considered, on the other hand, as a combination of ferric cyanide with three molecules of potassium cyanide, that is, $Fe(CN)_3 + 3KCN$.

As in the case of the dissection of the alum formula (p. 547), this must not be considered as meaning that these two bodies, the ferrocyanide and the ferricyanide, are mere mechanical combinations of cyanides of potassium and iron, for in both cases there is an intimate combination between the cyanogen group, the iron, and the potassium, as is best shown in the appended graphic formulas:

Potassium ferrocyanide.



Potassium ferricyanide.



As already mentioned on p. 556, the chief pharmaceutic value of these two bodies is as tests for the iron compounds, the ferrocyanide giving blue precipitate with ferric salts and the ferricyanide giving blue only with ferrous salts.

Cyanic Acid ($HCNO$).—This differs from hydrocyanic acid in containing one atom of oxygen. It in itself possesses no pharmaceutic interest. Its ammonia salt, however, ammonium cyanate, NH_4CNO, is of interest as the product from which urea was first made synthetically (p. 756).

Thiocyanic Acid, or *Sulphocyanic Acid,* $HCNS$, yields the potassium thiocyanate, $KSCN$, which is recognized in the Pharmacopœia in the form of a test solution, it being the most delicate test for iron, a drop of the solution giving a clear red tint to a liquid containing the merest trace of a ferric salt.

Mercuric Thiocyanate, $Hg(CNS)_2$, is the chief constituent of the dangerous fireworks, "Pharaoh's serpents," these being a mixture of mercury salt with starch or other excipient. When ignited it swells to enormous proportions, forming shapes somewhat similar to serpents. One of the products of the burning, however, is hydrocyanic acid, and their use by children should be prohibited.

Sodii Thiocyanas (N.F. VI), $NaCNS$, and **Potassii Thiocyanas** (N.F. VI), $KCNS$, have recently enjoyed great vogue as remedies for mental disorders. These thiocyanides possess little toxicity being administered in 5 grain doses.

As the organic cyanides possess isomeres which were called isonitriles, so thiocyanic acid possesses an isomere, isothiocyanic acid, the two differing in exactly the same way as the two nitriles, as shown in graphic formulas given below:

Thiocyanic acid.

$$H—C \equiv N = S$$

Isothiocyanic acid.

$$H—N = C = S$$

The allyl ester of isothiocyanic acid, C_3H_5NCS, is interesting as the chief constituent of oil of mustard.

OLEUM SINAPIS VOLATILE—Volatile Oil of Mustard

(Ol. Sinap. Vol.—Mustard Oil)

Volatile Oil of Mustard is the oil obtained by maceration with water and subsequent distillation of the dried ripe seed (free from fixed oil) of *Brassica nigra* (Linné) Koch or of *Brassica juncea* (Linné) Cosson (Fam. *Cruciferæ*), or prepared synthetically.

Volatile Oil of Mustard yields not less than 93 per cent of allyl isothiocyanate (C_3H_5NCS).

Volatile Oil of Mustard must be labeled to indicate whether it was made synthetically or distilled from either of the plants mentioned above.

Caution.—Great care must be exercised in smelling this oil. It should be tasted only when highly diluted.

Storage.—Preserve in well-closed containers.

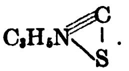
Summarized Description.

Colorless, pale-yellow, strongly refractive liquid; very pungent odor; terribly irritating; sp. gr. 1.013 to 1.020; optically inactive; distils between 148° and 154° C. For details, see U.S.P., p. 268.

For *tests for identity,* for *impurities* (alcohol, chloroform, petroleum or fatty oils, phenols) and for assay, see U.S.P., p. 269.

Composition.—Chiefly allyl isothiocyanate, $CH_2{=}CH—CH_2NCS$, and some propenyl-isothiocyanate, $CH_3CH{=}CHNCS$.

Dadieu inclines to the idea that the formula of allyl-isothiocyanate is



Remarks.—The manufacture of this volatile oil given in the above official definition will be explained below, when considering constituents of *black mustard.* Oil of mustard is one of the most violently irritating of volatile oils, even pouring of the oil from one bottle to another producing serious irritation to the mucous membrane of the eye and nose, hence the pharmacopœial caution as to smelling.

The assay, based as it is on the behavior of volumetric solution of silver nitrate, will be explained along with that testing liquid (p. 1020).

Medical Properties.—A powerful irritant, used almost exclusively externally as a rubefacient.

Dose.—0.008 cc. (1/8 minim).

SINAPIS NIGRA—Black Mustard

(Sinap. Nig.—Brown Mustard)

Black Mustard is the dried ripe seed of *Brassica nigra* (Linné) Koch or of *Brassica juncea* (Linné) Cosson or of varieties of these species (Fam. *Cruciferæ*).

Black mustard contains not more than 5 per cent of other seeds or other foreign organic matter, and yields not less than 0.6 per cent of volatile oil of mustard (calculated as allyl isothiocyanate).

Constituents.—Fixed oil, 25 per cent, the glucoside, *sinigrin,* or *potassium myronate;* the ferment, *myrosin;* mucilage, proteids, etc.

Remarks.—Under glucosides (p. 714) the equation showing the hydrolysis of the glucoside, potassium myronate, into glucose, potassium bisulfate, and allyl isothiocyanate is given. Here let it be added that the latter substance constitutes the bulk of the volatile oil of mustard. This oil is not found in the dry seed, but is produced when the dry powder is moistened with water by the reaction between the glucoside, potassium myronate, and the enzyme, myrosin, both substances occurring in the seed; that black mustard yields its fixed oil on expression, that after the fixed oil is pressed out, the dry squeezed mass, on moistening with water, yields volatile oil by the induced action of enzyme on glucoside; and, finally, that the official volatile oil of mustard is obtained by distillation of the moist pulp.

In preparing "mustard leaves," as they are usually called (see Mustard Plaster, p. 378) the ground mustard is first percolated with benzin. This solvent extracts the fixed oil, which, if allowed to remain, would grease the paper on which the mustard is spread. Mustard plasters can be prepared extemporaneously by mixing powdered mustard with water and spreading on a cloth. The water used in moistening this or the ready-made mustard leaves must be cold, not hot, as hot water destroys the activity of the enzyme, myrosin, preventing the formation of volatile oil.

Medical Properties.—Condiment, emetic, rubefacient. Official preparation, *mustard plaster* (p. 378).

Dose.—As an emetic, 10 Gm. (2½ drachms).

Sinapis Alba (U.S.P. IX), or *White Mustard,* is the seed of *Sinapis alba.* It contains 25 per cent of fixed oil; the glucoside, *sinalbin,* $C_{30}H_{44}N_2S_2O_{61}$, which hydrolyzes under influence of the ferment myrosin into dextrose, *acrinyl thiocyanate;* and *sinapin bisulfate* (the last two giving white mustard its activity); proteids; mucilage; *sinapin thiocyanate,* etc.

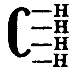
The activity of white mustard, like that of black mustard, depends on a sulfurated volatile oil, and likewise is produced by the hydrolysis of a glucoside. It is important to note, however, that neither the glucoside nor the volatile oil has the same composition as those found in black mustard.

The powdered English mustard used as a condiment possesses a bright yellow tint, while the official mustards, when powdered, are from gray to green-brown. The bright hue of the English article is due to admixture with turmeric, an addition that can scarcely be considered in this case as an adulteration. White mustard has the same medical properties as black mustard and is given in the same doses.

CARBONIC ACID DERIVATIVES

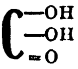
As hydrocyanic acid is considered as a methane in which three of the hydrogens are replaced by one nitrogen atom, so can carbonic acid be considered as methane, in which two of the hydrogens are replaced by two hydroxyls and two by one atom of oxygen, while formic acid can be considered as methane in which one of the hydrogen atoms is replaced by hydroxyl, and two by one atom of oxygen, as can best be shown by the graphic formulas given below:

Methane.



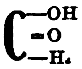
$$C\begin{matrix}-H\\-H\\-H\\-H\end{matrix}$$

Carbonic acid.



$$C\begin{matrix}-OH\\-OH\\=O\end{matrix}$$

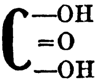
Formic acid.



$$C\begin{matrix}-OH\\=O\\-H.\end{matrix}$$

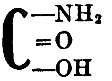
Taking the graphic formula of carbonic acid given above as a type, we find several organic bodies which can be considered as direct derivatives thereof. For example, by replacing two hydroxyl groups by chlorine we get a body, $COCl_2$, which is called *carbon oxychloride*, or more generally, *phosgene*. This body is made by oxidation of chloroform with chromic acid, and occasionally chloroform decomposes with its formation (particularly under the action of gas or lamp light), in which case the chloroform is, of course, dangerous for inhalation, as explained on p. 646. As a "poison gas" it is made by passing chlorine and carbon monoxide over heated wood charcoal. The hydroxy groups of carbonic acid can be replaced by other bodies—for example, the amido group, NH_2. Thus, carbonic acid in which one of the hydroxyl groups is replaced by an amido group gives us carbamic acid, while if the two hydroxyl groups are replaced by two amido groups, we obtain urea. This can best be explained by examination of the graphic formulas given below:

Carbonic acid.



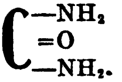
$$C\begin{matrix}-OH\\=O\\-OH\end{matrix}$$

Carbamic acid.



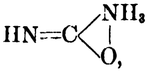
$$C\begin{matrix}-NH_2\\=O\\-OH\end{matrix}$$

Urea.



$$C\begin{matrix}-NH_2\\=O\\-NH_2.\end{matrix}$$

Werner believes that the time-honored formula for urea given above is wrong and that its structure is best expressed as:



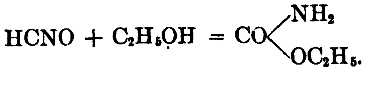
$$HN{=}C\begin{matrix}\diagup NH_3\\ \mid\\ \diagdown O,\end{matrix}$$

that is, with one nitrogen having the valence three, the other having the valence five.

Carbamic acid is of interest as being a constituent of the official ammonium carbonate, as explained on p. 505.

Æthylis Carbamas (U.S.P. IX) or *Ethyl Carbamate*, commonly called *urethane*, is the ethyl ester of carbamic acid, the formula being $CO\begin{matrix}\diagup NH_2\\ \diagdown OC_2H_5\end{matrix}$. It was discovered by Dumas in 1833, and is made by treating phosgene with alcohol and converting the resulting body, the ethyl ester of chlorocarbonic acid, $CO\begin{matrix}\diagup Cl\\ \diagdown OC_2H_5\end{matrix}$, into urethane by treatment with ammonia gas.

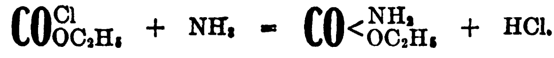
It is also prepared by treating cyanic acid with alcohol:



$$HCNO + C_2H_5OH = CO\begin{matrix}\diagup NH_2\\ \diagdown OC_2H_5.\end{matrix}$$

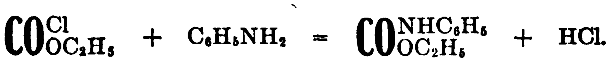
It occurs in colorless crystals or scales, and is used as a hypnotic. *Dose.*—1 Gm. (15 grains).

Euphorin is phenyl urethane, shown by formula $CO\begin{matrix}\diagup NHC_6H_5\\ \diagdown OC_2H_5.\end{matrix}$ It will be seen above that urethrane is made by treatment of the ethyl ester of chlorocarbonic acid with ammonia gas:



$$\mathrm{CO}\genfrac{}{}{0pt}{}{\mathrm{Cl}}{\mathrm{OC_2H_5}} + \mathrm{NH_3} = \mathrm{CO}<\genfrac{}{}{0pt}{}{\mathrm{NH_2}}{\mathrm{OC_2H_5}} + \mathrm{HCl}.$$

If, instead of ammonia, aniline is used, euphorin results:



$$\mathrm{CO}\genfrac{}{}{0pt}{}{\mathrm{Cl}}{\mathrm{OC_2H_5}} + \mathrm{C_6H_5NH_2} = \mathrm{CO}\genfrac{}{}{0pt}{}{\mathrm{NHC_6H_5}}{\mathrm{OC_2H_5}} + \mathrm{HCl}.$$

Euphorin is used as an antithermic, antirheumatic, and antiseptic.

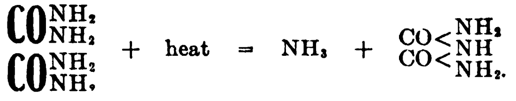
Ural is chloral urethane and is hypnotic, as is also **somnal, ethylated ural**, this being made by treating chloral with alcohol and urethane.

Urea (N.N.R.), $\mathrm{CO(NH_2)_2}$, is a normal constituent of the urine, and was found therein in 1773 by Rouelle. Its chief interest is based on the fact that its manufacture was the first organic synthesis performed, this historic work being performed by Wohler in 1828 by heating ammonium cyanate. Urea is now being prepared synthetically in lots of 1 ton or over. One method followed is by combining ammonia and carbon dioxide at 135° C. and under 100 atmospheres pressure. In another process, it is made by combining lime, carbon, nitrogen from the air in an electric furnace; followed by treatment with water. It is now being produced so cheaply that it is being used to a certain extent as a fertilizer.

Urea is now used as a diuretic.

By heating urea, *biuret* is obtained by the following reaction:

Two molecules urea. Ammonia. Biuret.

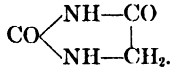


$$\begin{matrix}\mathrm{CO}\genfrac{}{}{0pt}{}{\mathrm{NH_2}}{\mathrm{NH_2}}\\ \mathrm{CO}\genfrac{}{}{0pt}{}{\mathrm{NH_2}}{\mathrm{NH_2}}\end{matrix} + \text{heat} = \mathrm{NH_3} + \begin{matrix}\mathrm{CO}<\genfrac{}{}{0pt}{}{\mathrm{NH_2}}{\mathrm{NH}}\\ \mathrm{CO}<\mathrm{NH_2}.\end{matrix}$$

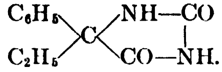
Biuret, when treated with the proper quantities of copper sulfate and potassium, hydroxide solutions gives the characteristic violet-red color, hence the so-called "biuret" reaction of urea produced on heating urine with these chemicals.

Pollopas is the trade name given to a condensation product of urea and formaldehyde. It is a colorless transparent substance that has been tried (without much success) as substitute for ordinary glass.

Hydantoin is a product of the condensation of urea and glycolic acid ($\mathrm{CH_2OH—COOH}$). It occurs in colorless needles and is of pharmaceutical interest because of the use of some of its derivatives as hypnotics. Its graphic formula is:

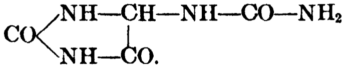


Nirvanol is *phenyl-ethyl-hydantoin*,



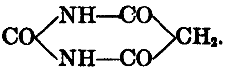
It occurs in colorless needles melting at about 200° C. It is used as a hypnotic in 1-Gm. doses.

Allantoin, is the diureide of glyoxylic acid. Its formula is



It is found in the old folk-medicine, comfrey, and is claimed to be responsible for the healing action of maggots used in the modern treatment of wounds.

Barbituric Acid is a condensation product of urea and malonic acid, $\mathrm{CH_2(COOH)_2}$. Its graphic formula is

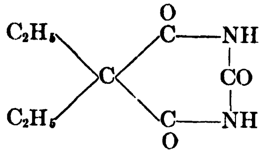


It occurs in large colorless prisms and is of pharmaceutical interest because a number of its derivatives are now in popular use as hypnotics.

BARBITALUM—Barbital

(**Barbital.**—Diethylbarbituric Acid, Barbitone, Diethylmalonylurea)

$C_8H_{12}O_3N_2$



Molecular weight, 184.11

Summarized Description.

Colorless or white crystals or white powder; odorless; slightly bitter; soluble in about 130 parts of water, about 12 parts of alcohol, about 113 parts of chloroform and about 25 parts of ether; melts between 187° and 190° C. For details, see U.S.P., p. 80.

For *tests for identity* and for *impurity* (carbonizable substances), see U.S.P., p. 81.

Remarks.—This official is the largely used hypnotic *veronal.* Its graphic formula is given above.

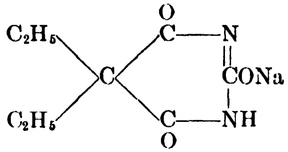
It is made by interaction of the esters of diethylmalonic acid with urea in the presence of metallic alcoholates. Veronal is a white crystalline powder, melting at 188° C. and soluble in 130 parts of water.

Dose.—300 mg. (5 grains).

BARBITALUM SOLUBILE—Soluble Barbital

(**Barbital. Sol.**—Barbital Sodium, Sodium Diethylbarbiturate, Soluble Barbitone, Sodium Diethylmalonylurea)

$C_8H_{11}O_3N_2Na$



Molecular weight, 206.10

Soluble Barbital, when dried to constant weight at 100° C., yields not less than 88 per cent, and not more than 90 per cent of barbital ($C_8H_{12}O_3N_2$).

Summarized Description.

White powder; odorless; bitter taste; soluble in about 5 parts of water; slightly soluble in alcohol; insoluble in ether. For details, see U.S.P., p. 81.

For *tests for identity,* for *impurities* (carbonizable substances, chloride, sulfate, heavy metals) and for *assay,* see U.S.P., p. 82.

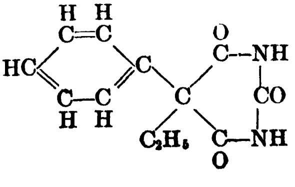
Remarks.—Barbital sodium has all of the hypnotic value of barbital with the added advantage of greater solubility in water. It is incompatible with chloral hydrate; the sodium ion of barbital compound breaking up the chloral into a formate (p. 667). Maloney and his associates find picrotoxin, administered intravenously; is useful as an antidote.

Dose.—300 mg. (5 grains).

PHENOBARBITALUM—Phenobarbital

(**Phenobarb.**—Phenylethylmalonylurea, Phenobarbitone)

$C_{12}H_{12}O_3N_2$



Molecular weight, 232.11

Phenylethylbarbituric acid.

Summarized Description.

White glistening crystals or white powder; odorless; soluble in about 1000 parts of water, about 7 parts of alcohol, about 60 parts of chloroform, about 10 parts of ether and about 617 parts of benzene; melts between 173° and 177° C. For details, see U.S.P., p. 283.

For *test for identity* and for *impurities* (carbonizable matter, phenylbarbituric acid), see U.S.P., p. 283.

Remarks.—This official, largely sold under the trade-marked name, *luminal*, has the formula given above.

Comparison of formulæ will show its close resemblance to barbital, which has just been described. The presence of the phenyl (C_6H_5) group, however, increases its activity and this is reflected in the much smaller doses in which it is administered as a hypnotic.

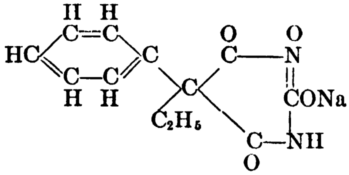
These barbituric acid compounds, originally exploited as "nonhabit-forming" hypnotics, are now known to produce addiction. Modern drug legislation tends to include them among the narcotic drugs.

Dose.—30 mg. (½ grain).

PHENOBARBITALUM SOLUBILE—Soluble Phenobarbital

(Phenobarb. Sol.—Phenobarbital Sodium, Soluble Phenobarbitone)

$C_{12}H_{11}O_3N_2Na$



Molecular weight, 254.10

Soluble Phenobarbital, when dried at 140° C. for six hours, contains not less than 90.4 per cent and not more than 91.4 per cent of phenobarbital ($C_{12}H_{12}O_3N_2$).

Summarized Description.

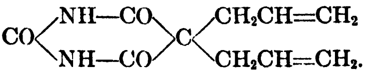
Flaky hygroscopic crystals or white, crystalline granules or white powder; odorless; bitter taste; very soluble in water, soluble in alcohol, almost insoluble in ether and chloroform.

For *tests for identity*, for *impurities* (soluble barbital, phenobarbital, chloride, sulfate, heavy metals, carbonizable substances) and for *assay*, see U.S.P., p. 284.

Remarks.—This is monosodium salt of phenylethylbarbituric acid. It is used like phenobarbital, but has the advantage of being very soluble in water.

Dose.—30 mg. (½ grain).

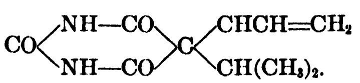
Dial is *diallylbarbituric acid:*



$$\mathrm{CO}\left\langle\begin{matrix}\mathrm{NH{-}CO}\\ \mathrm{NH{-}CO}\end{matrix}\right\rangle\mathrm{C}\left\langle\begin{matrix}\mathrm{CH_2CH{=}CH_2}\\ \mathrm{CH_2CH{=}CH_2}\end{matrix}\right..$$

It is used as a hypnotic in 100- to 300-mg. doses.

Allonal is *allylisopropylbarbituric acid:*



$$\mathrm{CO}\left\langle\begin{matrix}\mathrm{NH{-}CO}\\ \mathrm{NH{-}CO}\end{matrix}\right\rangle\mathrm{C}\left\langle\begin{matrix}\mathrm{CHCH{=}CH_2}\\ \mathrm{CH(CH_3)_2}\end{matrix}\right..$$

As marketed however it is a mixture of true allonal and amidopyrine (p. 765).

There are a number of other urea derivatives used in modern medicine. Among these is one official substance, *carbromal.*

CARBROMALUM—Carbromal
(Carbrom.)

$C_7H_{13}O_2N_2Br$ $(C_2H_5)_2.CBr.CO.NH.CONH_2$ **Molecular weight, 237.03**

Bromdiethylacetylurea.

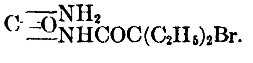
Summarized Description.

White crystalline powder; odorless; soluble in about 3000 parts of water, about 15 parts of alcohol, about 5 parts of chloroform and about 11 parts of ether; soluble in concentrated acids and solutions of alkaline hydroxides; melts between 116° and 119° C.

For details, see U.S.P., p. 110.

For *tests for identity* and for *impurities* (carbonizable matter, chloride, sulfate), see U.S.P., p. 110.

Remarks.—This official, largely sold under the trade-marked name, *adalin*, has the formula

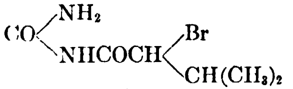


$$C{=}O\begin{array}{l}\text{—NH}_2\\ \text{—NHCOC}(C_2H_5)_2\text{Br.}\end{array}$$

That is, it is acetylurea with the three hydrogens of the methyl group replaced by two ethyl groups and one atom of bromine. It is a popular hypnotic.

Dose.—500 mg. (8 grains).

Bromural (N.N.R.) is *monobromisovalerylurea:*



$$CO\begin{array}{l}\diagup NH_2\\ \diagdown NHCOCH\begin{array}{l}\diagup Br\\ \diagdown CH(CH_3)_2\end{array}\end{array}$$

It is used as a nerve sedative in 300-mg. doses.

Iodival is *iodoisovalerylurea.* It contains 47 per cent of iodine and is used instead of potassium iodide as a neurotrophic and sedative in asthma and arteriosclerosis. *Dose.*—300 mg.

Afenil (N.N.R.) is a molecular compound of calcium chloride and urea. It is intended for intravenous injections for hay fever and asthma. It is dispensed in ampuls containing 10 cc. of a 10 per cent solution. Two or 3 injections of 10 cc. each are employed in hay fever.

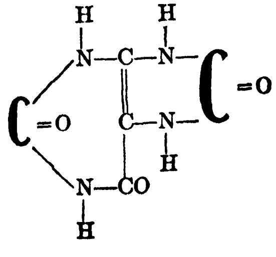
Uric acid was discovered by Scheele in 1776, and is found as a constituent of the urine and of the excrement of serpents. It is made synthetically, but the synthesis is of interest only as establishing its graphic formula, which is given below.

It is generally prepared from *guano*, the dried dung of sea birds.

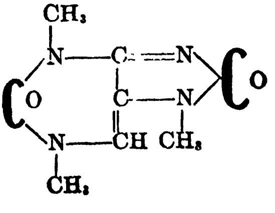
Uric acid is interesting to us because of the similarity of its formula to that of the well-known so-called "alkaloids," "theobromine," "theophylline," and "caffeine," as is shown by the comparison of the four formulas printed below.

Caffeine is uric acid in which three hydrogen atoms are replaced by three methyl (CH_3) groups, and with the central CO group changed to CH; while theobromine and theophylline contain only two methyl groups.

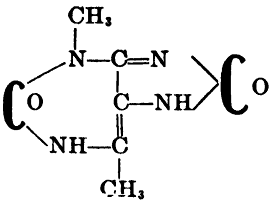
Uric acid.



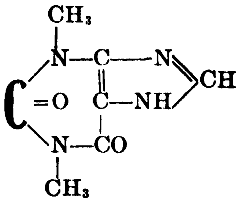
Caffeine.



Theobromine.

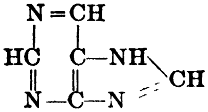


Theophylline.

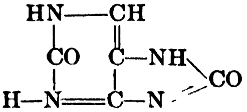


Fischer, in his classic research on these bodies, considers them not so much as allies of uric acid, but as derivatives of purine and of xanthine. His formulæ for these two bodies are:

Purine.



Xanthine.

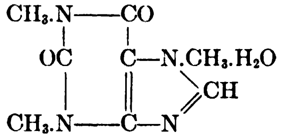


Comparison of these two formulæ with the four given above show that their difference is only one of configuration. The structural formulæ of U.S.P. XI (given below) show slightly different formation to those given above.

CAFFEINA—Caffeine

(Caff.)

$C_8H_{10}O_2N_4.H_2O$



Molecular weight, 212.13

Trimethylxanthine.

Storage.—Preserve in well-closed containers.

Summarized Description.

White, flexible, silky, glistening needles, usually in fleecy masses; bitter taste; efflorescent; soluble in about 46 parts of water, in about 53 parts of alcohol, also in chloroform, in ether and in benzene; melts between 235° and 237° C. For details, see U.S.P., p. 92.

For *tests for identity,* for *impurities* (carbonizable matter, alkaloids), see U.S.P., p. 93.

Color Test.—Treat caffeine with hydrochloric acid and potassium chlorate. Dried residue treated with ammonia fumes turns purple. For details, see U.S.P.

Manufacture.—Made chiefly from the dust and sweepings of tea leaves; treating a decoction of same with lead acetate, precipitating excess of lead with hydrogen sulfide, and finally concentrating solution to point at which it crystallizes

It can also be made from tea, coffee, or guarana by cooking with litharge and water, precipitating excess of lead with hydrogen sulfide, and crystallizing. As the yield from coffee is small (0.87 to 2.0 per cent), tea sweepings (1.5 per cent to 3 per cent) or guarana (5 per cent) are generally used.

An important commercial source of caffeine of today is the by-product obtained in preparing "caffeineless" coffee, now so largely used by health faddists.

Remarks.—Caffeine, formerly considered an alkaloid, is now, as mentioned above, considered as a feebly basic principle. It differs from alkaloids in not being precipitated by potassio-mercuric iodide. Like alkaloids, it forms combinations with acids, but these possess such weak union that the Pharmacopœia, in the case of the one official acidulated compound, that with citric acid, does not call it caffeine citrate, but citrated caffeine.

Dose.—**200 mg. (3 grains).**

CAFFEINA CUM SODII BENZOATE—Caffeine with Sodium Benzoate (Caff. c. Sod. Benz.—Caffeinæ Sodio-Benzoas U.S.P. X, Caffeine Sodio-Benzoate)

A mixture of caffeine and sodium benzoate, containing, when dried to constant weight at 80° C., not less than 47 per cent and not more than 50 per cent of anhydrous caffeine ($C_8H_{10}O_2N_4$); and not less than 50 per cent and not more than 53 per cent of sodium benzoate ($NaC_7H_5O_2$).

Storage.—Preserve in well-closed containers.

Summarized Description.

White powder; slightly bitter taste; soluble in about 1.1 parts of water (with slight decomposition), in about 24 parts of alcohol; partly soluble in chloroform; decomposed on strong heat, leaving a residue of sodium carbonate.

For details, see U.S.P., p. 94.

For *tests for identity*, and for *impurities* (carbonizable matter, heavy metals, chlorinated products), see U.S.P., p. 94.

Assay.—Similar to that for citrated caffeine. For details, see U.S.P., p. 95.

Remarks.—This caffeine compound contains from 47 to 50 per cent of that principle and is used because of its greater solubility in water. It is therefore used, when hypodermic injections of caffeine are indicated.

Dose.—By mouth, 300 mg. (5 grains). Hypodermic, 200 mg. (3 grains).

Caffeinæ Sodio-Salicylas (N.F. VI) is a mixture of equal amounts of caffeine and sodium salicylate and is used like the official sodio-benzoate preparation described above.

CAFFEINA CITRATA—Citrated Caffeine (Caff. Cit.)

A mixture of caffeine and citric acid containing, when dried to constant weight at 80° C., not less than 48 per cent and not more than 52 per cent of anhydrous caffeine ($C_8H_{10}O_2N_4$).

Storage.—Preserve in well-closed containers.

Condensed Recipe. (U.S.P. IX.)

Dissolve 50 Gm. citric acid in 100 cc. of hot distilled water, add 50 Gm. caffeine and evaporate to dryness on a water bath.

Summarized Description.

White powder; slightly bitter, acid taste; forms syrupy solution with small amount of water, precipitates caffeine on addition of more water, but makes a clear solution when still more water is added. For details, see U.S.P., p. 93.

For *tests for identity* and for *impurities* (tartrate, heavy metals, sulfate) and for *assay*, see U.S.P., p. 93.

Remarks.—Citrated caffeine, as given above, is made by blending caffeine with citric acid. The union is not a definite one, like the alkaloidal salts, hence the product is called "citrated," and not "citrate of."

It is chiefly used for making the effervescent salt.

Dose.—300 mg. (5 grains).

Caffeina Citrata Effervescens (U.S.P. IX), or *Effervescent Caffeine Citrate*, is made by a method similar to the other effervescent salts, viz., by rubbing the chemical (citrated caffeine in this case) with sodium bicarbonate, tartaric acid, and citric acid, softening mass by water-bath heat, and granulating by running through a coarse sieve. This product is a pleasant effervescent remedy for headache and nervous disorders, and is intended to replace the many proprietary preparations of similar character on the market.

Dose.—4 Gm. (60 grains).

Theobromine is the active constituent of *Theobroma Cacao*, and is obtained from the press cake of the cacao seed (after expressing the oil of theobroma) by mixing it with half its weight of slaked lime and boiling with 35 per cent alcohol. The crude theobromine obtained from the alcoholic solution is purified by recrystallization.

Theobromine sublimes at 290° C. without melting, and is so sparingly soluble in water that it has to be dispensed as the more soluble alkaline combinations, such as sodium theobromine. As these alkaline bodies are more or less irritating, double salts, such as diuretin, are to be preferred.

THEOBROMINA CUM SODII SALICYLATE—Theobromine with Sodium Salicylate

(Theobrom. c. Sod. Salicyl.—Theobrominæ Sodio-Salicylas U.S.P. X, Theobromine Sodio-Salicylate)

A mixture of sodium theobromine ($C_7H_7O_2N_4Na$) and sodium salicylate ($NaC_7H_5O_3$) in approximately molecular proportions. It yields, when dried to constant weight at 110° C., not less than 46.5 per cent of theobromine ($C_7H_8O_2N_4$) and not less than 35 per cent of salicylic acid ($HC_7H_5O_3$).

Storage.—Preserve in well-closed containers.

Summarized Description.

White odorless powder; sweetish, saline, somewhat alkaline taste; absorbs carbon dioxide from the air and liberates theobromine; soluble in about 1 part of water; aqueous solution should be colorless and not more than opalescent; ignites on heating, leaving a residue of sodium carbonate. For details, see U.S.P., p. 382.

For *tests for identity*, for *impurities* (caffeine, carbonate, carbonizable substances) and for *assay*, see U.S.P., p. 382.

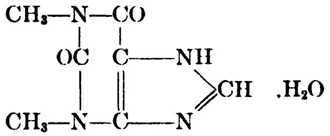
Remarks.—This official compound, usually sold under the trade name, *diuretin*, is sodium theobromine salicylate, and is made by combining 1 molecule of sodium theobromine with 1 molecule of sodium salicylate. It, therefore, should contain about 47 per cent theobromine. It occurs in a white powder, which is comparatively unstable in air, absorbing carbon dioxide and then breaking up and for this reason diuretin should never be dispensed in powder papers. It is given as a diuretic.

Dose.—1 Gm. (15 grains).

THEOPHYLLINA—Theophylline

(Theophyll.)

$C_7H_8O_2N_4.H_2O$



Molecular weight, 198.11

Summarized Description.

White crystalline powder, bitter taste; soluble in 120 parts of water and in 65 parts of alcohol, sparingly soluble in ether; melts between 269° and 272° C. For details, see U.S.P., p. 384.

For *tests for identity*, and for *impurities* (caffeine, theobromine, paraxanthin, carbonizable substances), see U.S.P., p. 384.

Remarks.—This official compound, which is isomeric with theobromine, is found in tea but is usually made synthetically by methylating uric acid. It is a white crystalline powder, sparingly soluble in water and is a powerful diuretic. One commercial form is sold under the name, ***theocine.***

Dose.—250 mg. (4 grains).

THEOPHYLLINA CUM SODII ACETATE—Theophylline with Sodium Acetate

(Theophyll. c. Sod. Acet.—Theophyllina et Sodii Acetas, Theophyllinæ Sodio-Acetas)

Theophylline with Sodium Acetate contains not less than 55 per cent and not more than 65 per cent of anhydrous theophylline ($C_7H_8O_2N_4$).

Storage.—Preserve in well-closed containers.

Summarized Description.

White crystalline powder, odorless, bitter, salty taste; soluble in 25 parts of water, insoluble in alcohol, in ether and in chloroform. For details, see U.S.P., p. 385.

For *tests for identity*, for *impurity* (caffeine) and for *assay*, see U.S.P., p. 385.

Dose.—200 mg. (3 grains).

THEOPHYLLINA CUM ÆTHYLENEDIAMINA—Theophylline with Ethylene Diamine

(Theophyll. c. Æthylenediam.—Aminophylline)

Theophylline with Ethylene Diamine contains, when dried over sulfuric acid for forty-eight hours, not less than 75 per cent and not more than 85 per cent of anhydrous theophylline ($C_7H_8O_2N_4$).

Storage.—Preserve in air-tight containers.

Summarized Description.

White or slightly yellowish granules, slight ammoniacal odor, bitter taste; soluble in 5 parts of water, insoluble in alcohol and in ether. For details, see U.S.P., p. 384.

For *tests for purity* and for *assay*, see U.S.P., p. 384.

Remarks.—These two new official diuretics, theophylline with sodium acetate or *theocin* and theophylline with ethylene diamine or *aminophyllin* have the advantage of theophylline of being more water-soluble.

Dose.—(Theocin) 200 mg. (3 grains). (Aminophyllin) 100 mg. (1½ grains).

PURINE DRUGS

There are a number of drugs that contain caffeine and similar bodies; three being recognized in N.F. VI.

Guarana (N.F. VI) is a dried paste made from the seed of *Paullinia Cupana.* It contains caffeine (4 to 5 per cent), paullitannic acid, gum, resin, volatile oil, etc.

Paullinia seed, ground up, made into a paste with water, rolled into cylinders, and dried, either by the sun or by the heat of a slow fire constitutes guarana. Its manufacture is in the hands of the Brazilian Indians, and is most primitive. The active ingredient of guarana is the same as that found in coffee and tea—the official caffeine. It is used as a stimulant and diuretic and is dispensed as the *fluidextract* (N.F.). The National Formulary also recognizes *elixir of guarana and celery* (p. 229). *Dose.*—2 Gm. (30 grains).

Kola (N.F. VI), the dried cotyledon of *Cola nitida*, has lately come into popularity as a stimulant. Kola contains caffeine; theobromine; kola-catechin, $C_{20}H_{20}O_8$; kolatin, $C_8H_{10}O_4$, crystals that oxidize to kola red; kolatein, a phenol, similar to phloroglucin. *Dose.*—60 grains.

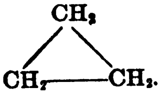
Coffea Tosta (N.F. V), the roasted seed of *Coffea arabica*, **tea,** the leaves of *Thea chinensis*, and **mate,** the leaves of *Ilex paraguayensis* also owe their activity to caffeine.

Chocolate, the ground seed of *Theobroma Cacao*, and *cocoa*, which represents the same seed exhausted of its fat (see oil of theobroma, p. 734) are well known as ingredients of beverages and confectionery. Besides the fat, chocolate contains theobromine, pentosans, enzymes, arabinose, galactose and glucose. The reddish-brown color of chocolate is due to *cacao red*, a pigment having the formula $(C_{34}H_{31}O_{13})x$. Cocoa is now being used extensively in pharmacy as a flavor and as a masker of the taste of bitter substances. It is official in N.F. VI. A recipe for *syrupus cacao* or *syrup of cocoa*, is given in the National Formulary.

SIMPLER RINGED COMPOUNDS

Up to this time we have considered compounds in which the carbon atoms are linked together, one after another, in the nature of the links of a chain, but even as the end links of a chain can be in turn linked, forming an endless chain or ring, so can end carbon atoms under certain circumstances be persuaded to link together, forming organic bodies of a ring nature.

We have already discussed the unsaturated chain compound, *Propylene*, $CH_2=CH—CH_3$, and from it can be made the isomeric *trimethylene*, having the formula



This represents the simplest ring.

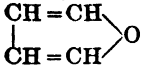
In **furane,** C_4H_4O, we have a ring of four carbon atoms in which the end carbon atoms, however, are not directly combined, but are linked by aid of an oxygen atom, as shown in graphic formula given below.

Furfural, C_4H_3OCHO, the aldehyde of furane, is now being produced from oat hulls in carload lots and is sold at about 10 cents a pound. It is used as a solvent in the nitrocellulose industry and in the manufacture of such products as shoe dyes, insecticides, and tree preservatives.

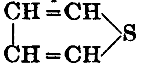
In **thiophene,** C_4H_4S, we have a similar body, in which the end carbon atoms are linked by aid of the sulfur atom.

Pyrrol, C_4H_4NH, is a similar body in which the end carbon atoms are attached by means of the NH group, these three being expressed below by graphic formulas:

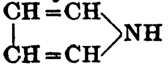
Furane.



Thiophene.



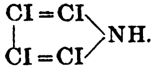
Pyrrol.



Of these three bodies, furane and thiophene are of little pharmaceutic interest, the latter substance being discovered by Victor Meyer as a constituent of benzene, with which, curious to relate, it has not merely been combined without discovery, but actually gave chemical test, which, for a long period, masqueraded as a test for the identity of benzene.

Pyrrol is of interest to us chiefly as the basis of one of the best known iodoform substitutes, *iodol.*

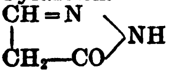
Iodol (U.S.P. VIII) discovered by Ciamician and Dennstedt in 1882, is tetra-iodopyrrol, as shown by the following formula:



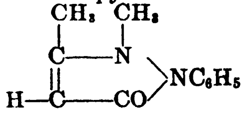
It is made by directly combining iodine with pyrrol, and has the highest iodine content of any organic substance save iodoform, and is greatly superior to that body in being devoid of its disagreeable odor. It is a useful antiseptic.

A body of composition similar to pyrrol is *pyrazol,* and a derivative of this, phenyldimethylpyrazolon, is the valuable synthetic, *antipyrine.* Below is given the formula of each of these substances for sake of comparison:

Pyrazolon.



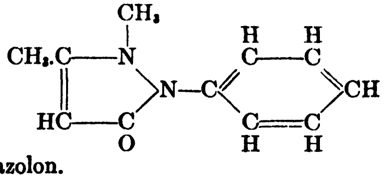
Antipyrine.



ANTIPYRINA—Antipyrine

(Antipyrin.—Phenazone)

$C_{11}H_{12}ON_2$



Molecular weight, 188.11

Phenyldimethylpyrazolon.

Summarized Description.

White crystalline powder or colorless crystals; slightly bitter taste; soluble in less than 1 part of water and in about one part of alcohol; in about 1.5 parts of chloroform and in about 30 parts of ether; melts between 111° and 113° C. For details, see U.S.P., p. 58.

For *tests for identity* and for *impurities* (heavy metals), see U.S.P., p. 58.

Remarks.—Antipyrine is made by treating ethyl-diacetic ester with phenylmethylhydrazine. It occurs in the form of a white powder, soluble in 1 part of water, and melting at about 113° C. Its most likely substitute, antifebrin, melts at about the same point, but it is interesting to note that antipyrine mixed with antifebrine does not melt at 113° C., but at 45° C., so the melting point is a valuable means of detecting admixture. When antipyrine is triturated with sodium salicylate or with chloral hydrate, it liquefies.

Antipyrine is one of the most valuable of the antipyretics. Its use is not free from danger, hence pharmacists should be careful in recommending it. In fact, it should not be administered except by direction of a physician.

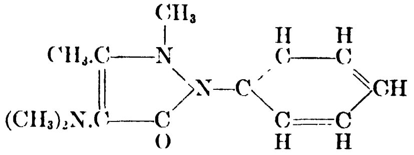
Dose.—300 mg. (5 grains).

The large demand for antipyrine gave rise to the manufacture of chemicals of similar character. Among these are *benzopyrine* (antipyrine benzoate), *salipyrine* (antipyrine salicylate), and *iodopyrine*, with an atom of iodine replacing an atom of hydrogen in phenyl compound.

AMINOPYRINA—Aminopyrine

(**Aminopyrin.**—Amidopyrina U.S.P. X)

$C_{13}H_{17}ON_3$



Molecular weight, 231.16

Dimethylaminophenyldimethylpyrazolon.

Summarized Description.

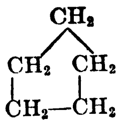
Colorless or white crystals or white powder; odorless; soluble in about 18 parts of water and about 1.3 parts of alcohol; also soluble in benzene, chloroform and ether; melts between 107° and 109° C. For details, see U.S.P., p. 51.

For *tests for identity* and for *impurities* (antipyrine, carbonizable matter, heavy metals, chloride), see U.S.P., p. 52.

Remarks.—This official, largely sold under the trade-marked name, *pyramidon*, is antipyrine with one hydrogen atom of the pyrazolon nucleus replaced by a dimethylamino ($N(CH_3)_2$) group. Amidopyrine occurs in small colorless crystals soluble in about 18 parts of water. It is used as an antipyretic and anodyne.

Dose.—300 mg. (5 grains).

We have just mentioned ring compounds containing three and four carbon atoms respectively; a similar ring body, containing five carbon atoms, is pentamethylene:

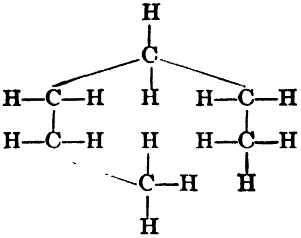


This is of no interest in pharmacy, and is merely mentioned as a step toward the ring compounds of real value—those possessing six carbon atoms.

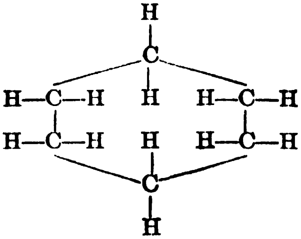
The saturated ring compound having six carbon atoms has the formula C_6H_{12}.

This body can be considered as hexane (C_6H_{14}) (Formula I), with a hydrogen atom removed from each end carbon atom, which are then linked by the free bonds, giving the structure shown in Formula II.

Formula I.



Formula II.

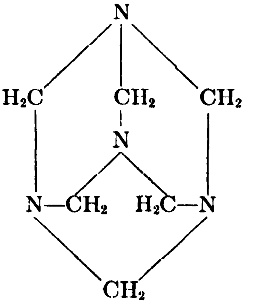


This body, C_6H_{12}, is called hexamethylene or hexahydrobenzene.

METHENAMINA—Methenamine

(Methenam.—Hexamethylenamine, Hexamethylenetetramine)

$C_6H_{12}N_4$



Molecular weight, 140.13

Methenamine contains not less than 99 per cent of $(CH_2)_6N_4$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless, lustrous crystals or white crystalline powder; soluble in about 1.5 parts of water, in about 10 parts of alcohol, in about 15 parts of chloroform and in about 230 parts of ether; sublimes at 263° C. without melting, partially decomposing. For details, see U.S.P., p. 233.

For *tests for identity* and for *impurities* (heavy metals, sulfate, chloride, ammonium salts) and for *assay*, see U.S.P., p. 233.

Remarks.—While hexamethylenetetramine can in some respects be best discussed at this place, from the purely chemical standpoint it might be better considered as a condensation product of formaldehyde, from which it is made. In truth, it has but little in common with hexamethylene, discussed above, its structure being quite different from that chemical, its graphic formula being given above.

Hexamethylenamine is usually dispensed as a crystalline powder, which liquefies when triturated with sodium benzoate. Tablets containing 5 or 7½ grains of this chemical burn with a hot flame and have actually been suggested as possible fuel.

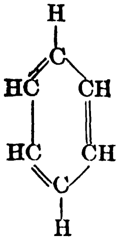
It is known in commerce as *cystogen*, *formin*, *urotropin*, etc., and is used as a uric-acid solvent and urinary antiseptic.

Dose.—300 mg. (5 grains).

Methenamine is produced on an enormous scale for use as a rubber vulcanization accelerator. A large number of other organic chemicals are now being used for the same purpose.

From hexamethylene (C_6H_{12}) it is but a simple step (theoretically) to benzene, C_6H_6 (or benzol).

If from the graphic formula of hexamethylene given above the six hydrogen atoms inside the hexagon are removed, and freed bonds of the carbon atoms are linked, we get the formula of benzene:



Observe that in this formula we have a hexagon or ring of six carbon atoms, each linked to one neighbor by one bond, and to the other by two or by "a double bond," as we say. We have stepped from the fatty to the aromatic hydrocarbons—from the chain to the ring series.

BIBLIOGRAPHY

Cyanogen.—Readman, Jl. Soc. Ch. Ind., 8, 1889, 757.

Paracyanogen.—Diehl, A.Ph.A., 14, 1866, 251.

Hydrocyanic Acid.—(History) Bell, Ph. Jl., 1, 1841, 108. (Structural formula) Enklaar, C.A., 22, 1928, 191; Dadieu, C.A., 25, 1931, 874; Hanzlik and Richardson, Jl. A.Ph.A., 23, 1934, 751. (Preservation) Sadtler, A.J.P., 95, 1923, 273; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1154. (Tests) Ekeley and Macy, Jl. Soc. Ch. Ind., 42, 1923, 123A. (Antidote) Chen and co-workers, Jl. A.Ph.A., 24, 1935, 625.

Cyanides.—(Manufacture) Fownes, Ph. Jl., 1, 1842, 338.

Nitriles.—Desgrez, Comp. rend., 153, 1911, 895.

Ferro- and Ferricyanides.—(Structure) Deniges, Ch. News, 113, 1916, 214. (Manufacture) Brown, Henke and Miller, Jl. Soc. Ch. Ind., 39, 1920, 446A. (Tests) Mueller, C.A., 17, 1923, 699.

Thiocyanates.—Hofmann, B., 1, 1867, 28.

Sodium Thiocyanate.—Lang and Paterson, C.A., 26, 1932, 1031; Bancroft and Rutzler, C.A., 26, 1932, 1032

Oil of Mustard.—(Composition) Pomeranz, A., 351, 1907, 354; Mannich and Ritsert, B., 57B, 1924, 1116; Dadieu, B., 64B, 1931, 358. (Production) Lebaigue, Jl. de Ph., 8, 1868, 118.

Black Mustard.—(Sources) Winton and Bornemann, Jl. Ind. Eng. Ch., 9, 1915, 684. (Constituents) Will and Koerner, A., 125, 1863, 257; Gadamer, B., 20, 1887, 2322; Boutron and Fremy, Jl. de Ph., 26, 1840, 48 and 112; Sayre, A.J.P., 67, 1895, 339; Grimme, C.A., 7, 1913, 3039; Schneider and co-workers, C.A., 25, 1931, 1833.

White Mustard.—(Constituents) Robiquet and Boutron-Chalard, Jl. de Ph., 17, 1831, 279; Will and Laubenheimer, A., 199, 1879, 150; Gadamer, Arch. d. Pharm., 235, 1897, 83; Sayre, A.J.P., 67, 1895, 339; Lloyd, A.Ph.A., 46, 1898, 229. (Pharmacology) Van Leersum, C.A., 10, 1916, 2003.

Urethane.—(History) Dumas, Jl. de Ph., 20, 1834, 276. (Structure) Hodgkin, Ph. Jl. [3], 21, 1890, 301. (Manufacture) Engelhardt, Merck's Rep., 17, 1908, 20.

Euphorin.—Adler, A.Ph.A., 40, 1892, 977; Giacomini, A.J.P., 62, 1890, 389.

Ural.—Anon., A.Ph.A., 44, 1896, 479.

Somnal.—Radlauer, Am. Dr., 19, 1890, 6.

Phosgene.—Konowalow, C.A., 21, 1927, 4033; Jacqué, Jl. Soc. Ch. Ind., 47, 1928, 222B.

Carbamic Acid.—Divers, Jl. Ch. Soc., 23, 1870, 171.

Urea.—(General) Chattaway, Ch. News, 99, 1909, 121; Grimbert, Jl. de ph. et ch., 17, 1918, 271; Werner, Jl. Soc. Ch. Ind., 42, 1923, 736. (History) Raubenheimer, Jl. A.Ph.A., 17, 1928, 973. (Structural formula) Hendricks, Jl. Am. Ch. Soc., 50, 1928, 2461; Ebert, C.A., 25, 1931, 2696. (Manufacture) Ed., Jl. Ind. Eng. Ch., 20, 1928, 883; Klemenc, *ibid.*, News Ed., 8, July 10, 1930, 5; Clark and Gaddy, *ibid.*, 22, 1930, 1084. (Disguising taste) Eschenbrenner, Ph. Zt., 74, 1929, 93.

Uric Acid.—(Source) Cap and Henry, A.J.P., 12, 1840, 152; Bensch, A.J.P., 19, 1847, 80. (Structure) Liebig and Woehler, A., 26, 1838, 241. Fischer, B., 32, 1899, 435. (Test) Prout, Ann. chim. phys., [2], 10, 1819, 379.

Hydantoin Hypnotics.—Lumière and Perrin, 19, 1925, 375.

Barbituric Acid.—(Structure) Mulder, B., 6, 1873, 1234. (Derivatives) Dox and Jones, Jl. Am. Ch. Soc., 50, 1928, 2033. (Pharmacology) Lundy, Reprint, Anesthesia and Analgesia, Sept.–Oct., 1930. (Addiction) Anon., A.J.P., 100, 1928, 199; Coronedi, C.A., 22, 1928, 4649. (Incompatibilities) Rupp and Poggendorf, Apoth. Zt., 46, 1931, 503. (Antidote) Maloney and co-workers, C.A., 25, 1931, 4939.

Barbital.—Johnson, Jl. Ind. Eng. Ch., 10, 1918, 306; Stieglitz, Jl. A.Ph.A., 7, 1918, 742; Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 456.

Luminal.—Nolte and others, Yearbook, A.Ph.A., 9, 1920, 585; Hirschfelder, see above.

Dial.—Hirschfelder, see above.

Allonal.—Hirschfelder, see above.

Nirvanol.—Volweiler, Jl. Ind. Eng. Ch., 15, 1923, 908; Anon., A.Ph.A., Yearbook, 7, 1918, 163.

Theobromine.—(Preparation) Schmitt and Pressler, A., 217, 1883, 287; Donker, Trumann and Dragendorff, A.Ph.A., 28, 1880, 338; Mauersberger, Jl. Soc. Ch. Ind., 47, 1928, 210B. (Structure) Fischer, B., 30, 1897, 549. (Properties) Zernik, Ap. Zt., 21, 1906, 898; Wadsworth, Pharm. Era, 53, 1920, 241.

Diuretin.—Zernik (as above); Pawinski, A.Ph.A., 42, 1894, 717; Patta, C.A., 4, 1910, 950.

Caffeine.—(History) Schelenz, Ph. Zt., 55, 1910, 81. (Preparation) Stenhouse, A.J.P., 29, 1857, 68; Greene, A.J.P., 59, 1887, 337; Anon., Jl. Soc. Ch. Ind., 51, 1932, 1068. (Structure) Fischer, see above.

Caffeine Sodio-Salicylate.—Schoorl, C.A., 23, 1929, 3049.

Guarana.—(Preparation) Rusby, A.J.P., 60, 1888, 266. (Constituents) Berthemot and Dechastelus, Jl. de Ph., 26, 1840, 548. Greene, A.J.P., 49, 1877, 388. Hallowell, Ph. Jl. [3], 3, 1873, 773; Cooke, Ph. Jl., [3], 1870, 221; Bertrand and Carneiro, C.A., 25, 1931, 5505 and 26, 1932, 252. (Pharmacology) Anon., Am. Dr., 71, May, 1923, 25.

Kola.—(History) Christy, N. R., 10, 1881, 34; Dohme, A.J.P., 80, 1908, 411. (Constituents) Goris, C.A., 13, 1907, 2247; Ph. Jl., 86, 1911, 809 and Ber. Ph. Ges., 18, 1908, 345; Perrot and Goris, A.Ph.A., 56, 1908, 229; Casparis, C.A., 24, 1930, 5110.

Coffee.—(Constituents) Gorter, A., 358, 1907, 327; Sethness, C.A., 18, 1924, 1863.

Cacao.—(Production) Knapp, Jl. Soc. Ch. Ind., 43, 1924, 402 and 431; *ibid.*, 45, 1926, 140T; Stevens, C.A., 20, 1926, 1874; Blanck, Jl. Ind. Eng. Ch., 22, 1930, 358. (Constituents) Tollens and Maurenbrecher, A.Ph.A., 55, 1907, 905; Brill, C.A., 9, 1915, 3085; Jensen, Jl. Soc. Ch. Ind., 47, 1928, 290; Heiduschka and Bienert, C.A., 22, 1928, 595 and 3661; Adam and co-workers, Jl. Am. Ch. Soc., 53, 1931, 727; Freudenberg and co-workers, *ibid.*, 54, 1932, 1913. (Uses) White, A.Ph.A., 57, 1909, 1014.

Tea.—(Constituents) Paul and Cownley, Ph. Jl., [3], 18, 1887, 417; Kossel, A.J.P., 60, 1888, 462; Marshall, A.J.P., 75, 1903, 79; Deuss, C.A., 17, 1923, 3492 and 18, 1924, 1824; Carpenter and Harler, C.A., 18, 1924, 2022; Aoyama, C.A., 25, 1931, 5431; Tsujimura, C.A., 24, 1930, 5757; C.A., 25, 1931, 3637 and 4249.

Mate.—(Constituents) Peckolt, Ph. Jl., [3], 14, 1883, 121; Peacock, Proc. P.P.A., 45, 1923, 1173.

Furfural.—Killeffer, Jl. Ind. Eng. Ch., 18, 1926, 1217; Miner, Jl. Soc. Ch. Ind., 47, 1928, 120.

Pyrrol.—Ciamician, B., 37, 1904, 4200. Markwalder, Jl. prakt. Ch., 75, 1907, 329.

Iodol.—Ciamician and Dennstedt, B., 15, 1882, 2583; Ciamician and Silber, B., 18, 1885, 1766.

Thiophene.—Meyer, B., 16, 1883, 1465; Ardarg and Furber, Jl. Soc. Ch. Ind., 48, 1929, 73T.

Antipyrine.—(History) Arny, Jl. Ind. Eng. Ch., 18, 1926, 949. (Structure) Germuth, Jl. A.Ph.A., 19, 1930, 133. (Manufacture) Knorr, Am. Dr., 16, 1887, 164; Anon., Ch. and Dr., 85, 1914, 273. (Properties) Anon., Am. Dr. 18, 1889, 136; Prudhomme, Am. Dr., 18, 1889, 102; Blainville, Am. Dr., 18, 1889, 170. (Incompatibilities) Wood and Marshall, Am. Dr., 18, 1889, 87; Astruc and Vidal, C.A., 5, 1911, 3084; Weidenkopf, Ph. Era, 44, 1911, 241; Finnemore and Colverd, Yearbook, A.Ph.A., 5, 1916, 373; Paderi, C.A., 14, 1920, 2837; Lucas, C.A., 23, 1929, 3049.

Benzopyrine.—Crersati, A.Ph.A., 40, 1892, 1047.

Salipyrine.—Schulvien, Ph. Zt., 35, 1890, 395.

Iodopyrine.—Duroy, A.Ph.A., 40, 1892, 1049.

Hypnal.—Bardet, A.Ph.A., 38, 1890, 690.

Hexahydrobenzene.—Dougherty and Taylor, C.A., 17, 1923, 2872.

Naphthenes.—Beilstein and Kurbatow, B., 13, 1880, 1818.

Hexamethylenamine.—(History) Butlerow, A., 115, 1860, 322. (Manufacture) Wohl, B., 19, 1886, 1840. (Structure) Duden and Scharff, A., 288, 1895, 222; Dickinson and Raymond, Jl. Am. Soc., 45, 1923, 22. (Properties) Howell and Kyser, Jl. A.Ph.A., 6, 1917, 445. (Incompatibilities) Anon., C.A., 9, 1915, 2690; Fantus and Snow, Jl. A.Ph.A., 14, 1925, 791.

CHAPTER XLIII

THE AROMATIC SERIES

BENZENE AND ITS DERIVATIVES

Up to this page, Part IV has been devoted to the chain or fatty series, they being so called because a large number of their compounds were of fatty character. The next class of organic chemicals to consider is the aromatic series; so called because, among them, are found most of the aromatic substances in general use. All contain as a nucleus a ring compound, based on the benzene type of hydrocarbons. Those compounds like benzene (where the "ring" is made up of carbon atoms only) are called orthocyclic, while these containing in the "ring" elements other than carbon, like pyridine (p. 898), are called heterocyclic.

The graphic formula of benzene given in the preceding chapter is the one generally accepted, it answering best all the requirements of a body having the formula C_6H_6.

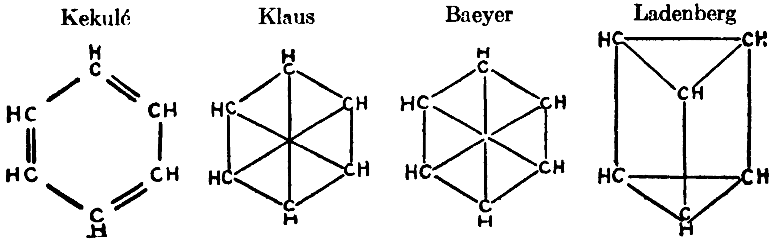
This formula is the one suggested by Kekulé, of Bonn, whose work on this very difficult subject has given him a place among the great chemists, and one of the most striking proofs of the truth of Kekulé's formula is the fact that it has withstood the criticism of seventy years, and remains to this day the most practical benzene formula that we have.

The chief difficulty of ascribing graphic formulas of the body C_6H_6 was found in reconciling the formula to the tetravalency of the carbon atoms. As shown on the preceding page, there is known a ring compound containing six carbon atoms united by single bonds. This means two hydrogen atoms attached to each carbon atom, a body having the formula C_6H_{12}. For a body to have the formula C_6H_6 means that every one of the six carbon atoms will have one set of double (unsaturated) bonds; a theory first advanced by Kekulé.

Other graphic formulas for benzene have been suggested, and these are pictured below. Thus, in Klaus' formula, the extra bonds of the carbon atoms are placed diagonally from carbon to carbon atom.

Baeyer considers these extra bonds as gravitating toward the center of the compound without forming a distinct union with any other bond, while Ladenberg assumes a totally different form, pictured below and called the prism form:

Benzene Formulas



Kekulé Klaus Baeyer Ladenberg

Each of these separate formulas has its advantages, and each shows some difficulties in reconciling them to the facts. And, after all the arguments are weighed, the time-honored Kekulé formula seems the most satisfactory.

During the last decade a number of new benzene formulas have been suggested. The most ingenious of these is a "space formula" proposed by Huggins and based upon the Bragg *x*-ray picture (see p. 169) of benzene crystals. The Huggins formula shows three tetrahedral carbon atoms (see p. 684) at the top of the hexagonal plane and the other three below the plane. For details the reader is referred to the articles cited in the Bibliography at the end of this chapter.

Benzene is what is commercially called benzol, preference being given to the first name, because of the desire to limit the termination "ol" to the alcohols. In this case the change is unfortunate, inasmuch as it leads to confusion between this aromatic body and the official benzin, which is a petroleum product, of character totally different from the benzene of which we are now speaking.

Benzene was discovered by Faraday in 1825. It was found in coal tar in 1845 by Hoffman, whose researches into the formation of dyestuffs was a wonderful impetus to the benzene industry. Benzene can be made by distilling benzoic acid with chalk, but now practically the entire output is from coal tar, that side product in the manufacture of coal gas from which so many valuable synthetics have been made in recent years. During the World War, benzene was prepared by "cracking" petroleum or paraffin, the "cracking" consisting in passing the petroleum through heated tubes under appropriate pressure.

Benzene is a colorless liquid boiling at 80° C. and solidifying between 5° and 6° C. Commercial benzol contains toluene and xylene and is sold as 30 per cent, 50 per cent or 90 per cent benzol according to its C_6H_6 content.

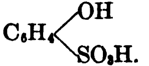
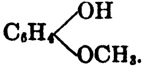
Benzene dissolves phenol whereas benzine does not. By treating benzene with concentrated nitric acid and subsequent distillation we are able to replace one of the hydrogens of benzene by an NO_2 group, giving us nitrobenzene, $C_6H_5NO_2$, which is commercially called *oil of mirbane,* and very erroneously called *artificial oil of bitter almond,* by reason of its somewhat similar odor. Oil of mirbane is used as a perfume for cheap soap.

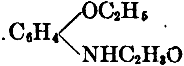
Benzene is used as a solvent and for making its more important derivatives. Recently it has enjoyed some vogue as a remedy in leukemia, being dispensed for this purpose in salol-coated enteric capsules.

It is distinctly poisonous. Its modern antidote is injections of a solution of acetylcholine.

When benzene is treated with chlorine two types of chlorinated compounds may result. Thus, one hydrogen of the C_6H_6 molecule may be replaced by chlorine, forming *monochlorbenzene,* C_6H_5Cl. Under different treatment, two atoms of chlorine may replace two atoms and hydrogen and *dichlorobenzene,* $C_6H_4Cl_2$, will result. This chemical is known in three isomeric forms, ortho-, meta- and para- forms (p. 775). *Paradichlorobenzene* is now largely used as an insecticide and moth repellent.

The following derivatives of benzene are of interest in pharmacy:

Phenol, U.S.P.	C_6H_6OH.
Liquefied phenol, U.S.P.	88 per cent solution of phenol.
Crude carbolic acid, U.S.P. 1890.	
Anisol	$C_6H_5—OCH_3$.
Phenolsulfonic acids (3 forms)	 $C_6H_4\begin{cases}OH\\SO_3H\end{cases}$.
Trinitrophenol, U.S.P.	$C_6H_2(NO_3)_3OH$.
Guaiacol, U.S.P.	 $C_6H_4\begin{cases}OH\\OCH_3\end{cases}$.
Guaiacol carbonate (U.S.P. X; N.F. VI)	$(C_6H_4OCH_3O)_2CO$.

Resorcinol, U.S.P.	$C_6H_4(OH)_2$.
Pyrogallol, U.S.P.	$C_6H_3(OH)_3$.
Aniline	$C_6H_5NH_2$.
Methylthionine chloride, U.S.P.	$C_{16}H_{18}N_3SCl.3H_2O$.
Acriflavine, U.S.P.	
Acriflavine hydrochloride, U.S.P.	
Acetanilid, U.S.P.	$C_6H_5NHC_2H_3O$.
Acetphenetidin, U.S.P.	 $C_6H_4\begin{smallmatrix}\diagup OC_2H_5\\ \diagdown NHC_2H_3O.\end{smallmatrix}$
Arsphenamine, U.S.P.	$HCl.NH_2.OH.C_6H_3As$: $AsC_6H_3.OH.NH_2.HCl$.
Neoarsphenamine, U.S.P.	$NH_2.OH.C_6H_3As$: $AsC_6H_3.OH.NH(CH_2O)O.S.Na$.
Merbaphen	$C_{16}H_{16}O_6N_2ClHgNa$.

MONATOMIC PHENOLS

Phenols are a class of alcohols peculiar to the benzene series, the hydroxyl being attached directly to the benzene nucleus, and its simplest example is the ordinary phenol, which is generally known as carbolic acid, and which can be considered as the hydroxide of *phenyl*, the latter word being the designation of the radical, C_6H_5. These phenols are like alcohols, inasmuch as they form ethers, an example of which is the phenyl methyl ether, $C_6H_5OCH_3$, commercially known as anisol, and, like the alcohols, form esters, an example of which is the official salol (phenyl salicylate). However, they are unlike the primary alcohols, inasmuch as they do not oxidize to aldehydes, and in most reactions will resemble the tertiary alcohols, it being a very difficult matter to oxidize same, although ketones are sometimes formed.

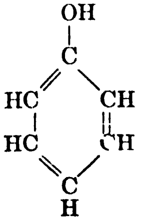
As stated above, the best known phenol is what is known as carbolic acid, and this is called an "acid" because it forms salts with the alkalis. From it, for example, we obtain sodium carbolate (C_6H_5ONa) and potassium carbolate (C_6H_5OK). It must be recalled, however, that even the alcohols of the chain series yield similar compounds, for instance, sodium alcoholate, C_2H_5ONa (p. 657). The carbolate, however, differs from the alcoholate, inasmuch as this can be made from carbolic acid by simply treating with alkali, whereas to make a sodium compound from alcohol requires treatment with the metal itself.

The phenols possess most of the reactions of the benzene nucleus from which they are derived; that is, the hydrogen of the benzene nucleus can be replaced by chlorine, the NO_2 group, and the like. An illustration of such a modified phenol is sodium phenolsulfonate, U.S.P. IX (p. 495).

PHENOL—Phenol

(Carbolic Acid)

C_6H_6O



Molecular weight, 94.05

Phenol contains not less than 98 per cent of C_6H_5OH.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, interlaced, needle-shaped crystals or white or light pink crystalline masses; characteristic, somewhat aromatic odor; strongly caustic, soluble in about 15 parts of water; very soluble in alcohol, glycerin, chloroform, ether, carbon disulfide and in fixed and volatile oils; melts when gently warmed; congeals at 39° C.; liquefies on addition of 8 per cent of water. For details, see U.S.P., p. 285.

For *assay,* see U.S.P., p. 285.

Remarks.—This, the original phenol, was discovered by Runge, in 1834, as a constituent of coal tar, from which it is separated by contact with potassium hydroxide (thus forming potassium carbolate), separation of the acid from potassium carbolate by treating with sulfuric acid and fractional distillation of the freed product. Carbolic acid is also made synthetically from benzene by conversion of benzene into sodium phenolsulfonate, $C_6H_5SO_3Na$, and fusing this with sodium hydroxide, when sodium carbolate and sodium sulfite are produced:

$$C_6H_5SO_3Na + 2NaOH = C_6H_5ONa + Na_2SO_3 + H_2O.$$

By treating the carbolate with acid, free phenol is obtained.

The official carbolic acid occurs in colorless, needle-shaped crystals having a characteristic odor and sweetish taste. It should, however, never be tasted in concentrated form.

The solubility of the crystalline phenol is a matter of interest. *One hundred parts dissolve eight parts of water* to a clear liquid. If more water be added, it clouds, since the acid will dissolve no more. This cloudiness is continued until 1500 parts of water have been added, when the conditions are reversed and the water dissolves the acid.

Some samples of crystalline phenol acquire a reddish tint on standing, and the origin of this disagreeable phenomenon has been a matter of considerable discussion. Some claim that the nitrogen of the air acts on the phenol, forming one of the numerous dye-stuffs obtained from benzene; others think it due to organic impurities, some think that copper contamination is the cause; while Gibbs states that it is due to the condensation of the phenol molecules to phenoquinone and other quinone derivatives. The removal of this color is a matter of considerable difficulty; the only perfect way is by the redistillation of the phenol, an operation that cannot be safely performed in the ordinary laboratory. It is claimed that a trace of tin salts prevent this discoloration.

It must be borne in mind that the vapors of phenol are inflammable, and, therefore, great care should be used in melting same by means of heat; in fact, the best way to melt the substance is to dip the bottle in heated water rather than to heat the mass direct, even on a water bath.

Phenol has a number of characteristic reactions, among which may be cited the violet-blue color it gives with a drop of ferric chloride solution, its coagulating action on collodion, and the white precipitate with bromine. The first two tests are of interest as distinguishing between itself and creosote, phenol being a frequent substitute for the more costly wood-tar product. The bromine reaction is of interest as the basis of the volumetric determination of phenol. (See Part V.)

When phenol is added to solution of lead subacetate a white precipitate is formed. According to Lum, this precipitate consists of lead phenoxide, $Pb(C_6H_5O)_2$.

As mentioned above, phenol can be liquefied by addition of 8 per cent of water. This solution, however, is scarcely so desirable as one liquefied by an addition of a small quantity of alcohol though even that may be objectionable on account of possible irritating qualities of the alcohol. This solution, the so-called "95 per cent phenol" is what is generally dispensed in answer to calls for pure phenol instead of the crystals themselves. The extended use of this 95 per cent carbolic acid by suicides, and the almost invariable fatal results from use in this way, has brought about legislation in several parts of this country prohibiting its sale except upon a physician's prescription.

Phenol is one of the most valuable of all antiseptics, its germicidal action being due to the fact that it coagulates albumin. In full strength it is, as mentioned above, a very caustic poison. The antidotes are syrup of lime, or a tumblerful of solution of potassium permanganate, 1 : 1000, or gastric lavage with 10 per cent alcohol. For phenol burns, the skin should be washed with alcohol, ether, glycerin, or oils. The latter should never be used internally as an antidote.

The official preparations of phenol are a 2 per cent *ointment.* The *glycerite,* which contains about 17 per cent of phenol, is recognized in the National Formulary. In some sections *carbolic oil,* made by combining phenol with either olive oil or cotton seed oil, in proportions from one to nineteen, is used for cuts and sores. The National Formulary recognizes this preparation under the title, *Oleum phenolatum.*

Dose.—60 mg. (1 grain).

PHENOL LIQUEFACTUM—Liquefied Phenol

(Phenol Liq.—Liquefied Carbolic Acid)

Phenol, maintained in the liquid condition by the presence of 10 per cent of distilled water. It contains not less than 88 per cent of C_6H_5OH.

Storage.—Preserve in well-closed containers and protected from light.

Condensed Recipe.

Liquefy phenol by heating an uncorked container on a water bath, then add 1 part of distilled water to each 9 parts of phenol. For details, see U.S.P., p. 286.

Summarized Description.

Colorless liquid, sometimes turning red on standing; characteristic, somewhat aromatic odor; very caustic, whitening skin and mucous membrane; miscible with alcohol, ether or glycerin; miscible with water only after admixture with glycerin; sp. gr. 1.065; boils not higher than 182° C. For details, see U.S P., p. 286.

For *tests for identity,* and for *assay,* see Phenol and also U.S.P., p. 286.

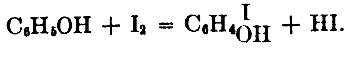
Remarks.—As mentioned under Phenol, that chemical forms a permanent liquid by the addition of from 8 to 10 per cent water, and this liquid has been given pharmacopœial recognition. Its use is, of course, the same as phenol.

Dose.—0.06 cc. (1 minim).

Phenol Iodatum (N.F. V), or *Iodized Phenol,* is made by warming together iodine (20 per cent), phenol (60 per cent) and glycerin.

Liquor Iodi Phenolatis (N.F. VI), or *Boulton's Solution,* is a colorless mixture made from liquefied phenol (6 cc. to the liter) compound solution of iodine, glycerin and water.

According to Krantz and Carr, the bleaching of the solution is due to the following reaction:



$$C_6H_5OH + I_2 = C_6H_4{}^{I}_{OH} + HI.$$

Both of these reaction products are colorless.

Phenol Camphoratum, or *Camphor-phenol,* contains 30 Gm. phenol, 60 Gm. camphor and enough liquid petrolatum to make 100 cc.

Formolites are synthetic resins obtained by the condensation of phenols with formaldehyde or its derivatives. The original is the well-known *Bakelite.*

Acidum Carbolicum Crudum (U.S.P. 1890).—*Crude carbolic acid* is a liquid consisting of various constituents of coal tar obtained by fractional distillation. The official crude carbolic acid is a nearly colorless or reddish or brownish-red liquid, and possesses a characteristic odor. The crude carbolic acid ordinarily sold in stores represents a very dirty black liquid, which has but little value, as it is notoriously weakened by addition of water. Crude carbolic acid is used entirely as a disinfectant, for which purpose it is better than the crystals, because it contains a large quantity of cresol in addition to its chief constituent, phenol.

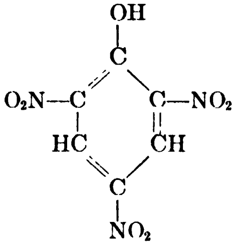
Anisol, $C_6H_5OCH_3$, as mentioned above, is phenylmethyl ether. We have already learned that if methyl alcohol and ethyl alcohol are combined in the presence of sulfuric acid, there will be yielded methylethyl ether, and in the same way if methyl alcohol and phenol are mixed in the presence of sulfuric acid, methylphenyl ether, or anisol, is produced. As its name suggests, it can be derived from oil of anise. During the World War, anisol was found to be a valuable remedy for body vermin.

As the consideration of methyl salicylate was deferred until we had discussed salicylic acid, it is consistent to refer the official *phenyl salicylate*, or *salol*, to the same heading.

TRINITROPHENOL—Trinitrophenol

(Trinitrophen.—Picric Acid)

$C_6H_2(OH)(NO_2)_3 1:2:4:6$



Molecular weight, 229.05

Storage.—Preserve in well-stoppered bottles, in a cool place, remote from fire.

Summarized Description.

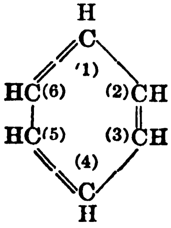
Pale-yellow, rhombic prisms or scales; intensely bitter taste; explosive; soluble in about 78 parts of water, in about 10 parts of alcohol, and also in chloroform, ether and benzene; melts between 121° and 123° C. For details, see U.S.P., p. 412

For *tests for identity* and for *impurity* (sulfate), see U.S.P., p. 412.

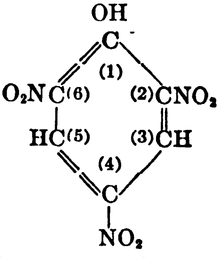
Remarks.—This substance is phenol in which three of the hydrogen atoms of the benzene nucleus are replaced by NO_2 groups, these groups replacing the hydrogen attached to carbon atoms two, four, and six respectively.

At this place it might be stated that, for sake of conciseness, chemists number the carbon atoms of the benzene ring as shown below:

Benzene.



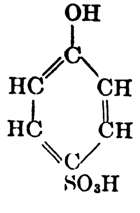
Picric acid.



Picric acid is made by treating trinitrobenzene with potassium ferricyanide. It appears in bright yellow crystals, soluble in water, having a strong acid character, and very explosive, hence should be handled by the pharmacist with the utmost care. It is used as a dye for silk, as an explosive and as reagent for alkaloids, albumin and sugar. In medicine, it is used occasionally as an antiperiodic. A 2 per cent hydro-alcoholic solution is popular as an application for burns, while a 5 per cent aqueous solution is said to be an excellent disinfecting wash.

Dose.—(U.S.P. X) 30 mg. (½ grain).

Sulfocarbolic Acid (or *Phenolsulfonic Acid*) is a body prepared by treating phenol with sulfuric acid. Its composition is best understood from the graphic formula:



The sodium salt of this acid is made by treating mixture of sulfuric acid and phenol with barium carbonate, whereby solution of barium sulfocarbolate is produced, and this solution, on being treated with a molecular quantity of sodium carbonate, produces sodium sulfocarbolate, while the barium is precipitated as barium carbonate. (See Sodium Compounds, p. 495.)

Sozoiodol represents sulfocarbolic acid in which two of the hydrogen atoms of the benzene nucleus have been replaced by iodine, and, indeed, those hydrogens attached to the carbon atoms number two and six. This is used as an antiseptic in the form of ammonium, barium, lead, and other metallic salts.

Sozol is a trade name for aluminum sulfocarbolate.

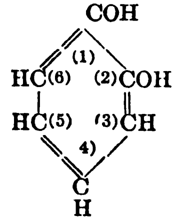
Aseptol is an aqueous solution of orthosulfocarbolic acid. This body differs from sulfocarbolic acid, mentioned above, in having the hydroxyl and sulfonic acid (SO_3H) groups on adjoining carbon atoms, this distinction between ortho-, meta-, and para-compounds being reserved for discussion below.

DIATOMIC PHENOLS

As we already learned when considering the fatty series, besides alcohols containing one hydroxyl, similar bodies have been found containing two, three, and even more hydroxyls, these being examples of polyatomic alcohols. Thus, glycerin, which, it will be recalled, has the formula $C_3H_5(OH)_3$, is a polyatomic or polyhydric alcohol. In the same way we can have polyatomic or polyhydric phenols.

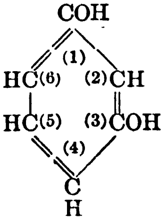
The simplest of these phenols are the diatomic—those possessing two hydroxyl groups. The direct benzene derivatives of this class have the formula $C_6H_4(OH)_2$, and with this, as with all di-derivatives of benzene, we have three types, based on the relative positions of the two substituted radicals. Taking $C_6H_4(OH)_2$ as example, we can best explain the three modifications by the graphic formulas given below:

Ortho-dihydroxybenzene.



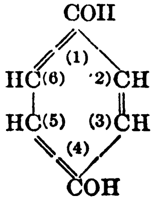
Pyrocatechin or catechol.

Meta-dihydroxybenzene.



Resorcin or resorcinol.

Para-dihydroxybenzene.



Hydroquinone or quinol.

It will be seen that the *ortho*-body is one in which the two hydroxyl groups are on adjoining carbon atoms; the *meta*- is the one in which one carbon atom intervenes between the two hydroxyl groups whereas the *para*-compounds have two carbon atoms intervening between the hydroxyl groups.

Possibly a clearer explanation of this is by numbering the carbon atoms as above, and saying that in the ortho-body the hydroxyl groups are attached to carbon atoms number one and two; in the meta-, the hydroxyl groups are attached to carbon atoms number one and three; and in the para-bodies, the hydroxyl groups are attached to carbon atoms number one and four.

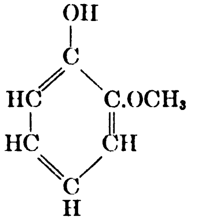
It is hardly necessary to note that this numbering is purely arbitrary, and that a benzene in which two radicals are attached to carbon atoms four and five would be as much ortho- as is that attached to one and two as given above.

Of the three diatomic phenols having the formula $C_6H_4(OH)_2$, the ortho-compound is called pyrocatechin; the meta-, resorcin, and the para-, hydroquinone.

Pyrocatechin, obtained by destructive distillation of catechin, is a constituent of catechu, U.S.P., 1890. It is of no pharmaceutic value. The methyl ether of same, however, is guaiacol.

GUAIACOL—Guaiacol

$C_7H_8O_2$



Molecular weight, 124.06

A liquid consisting principally of $C_6H_4(OH)(OCH_3)$1:2, usually obtained from wood creosote, or a solid, consisting almost entirely of $C_6H_4(OH)(OCH_3)$1:2, usually prepared synthetically.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless or yellowish, strongly refractive liquid or crystalline solid; agreeable aromatic odor; turns darker in exposure to light; soluble in about 70 parts of water and in about 1.25 parts of glycerin; miscible with alcohol, chloroform, ether or glacial acetic acid; sp. gr. of liquid form, 1.112; melting point of solid form, 28° C; at least 85 per cent distils between 200° to 210° C. For details, see U.S.P., p. 184.

For *tests for identity* and for *impurity* (hydrocarbons), see U.S.P., p. 184.

Remarks.—This substance can be made synthetically by heating pyrocatechin with a mixture of potassa and potassium methyl sulfate, although it is usually prepared commercially by the rectification of creosote.

Guaiacol is one of our most valuable internal antiseptics, and for this purpose is used both in tuberculosis and also in intestinal troubles.

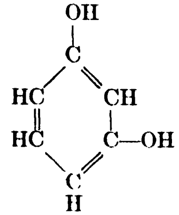
Dose.—0.5 cc. (8 minims).

Guaiacolis Carbonas (U.S.P. X; N.F. VI), or *Guaiacol Carbonate,* is an odorless and tasteless crystalline powder, that is soluble in about 48 parts of alcohol and insoluble in water. Its trade name is *duotal.* It is used like guaiacol but is less irritating. *Dose.*—1 Gm. (15 grains).

Potassii Guaiacolsulfonas (N.F. VI), or *Potassium Guaiacolsulfonate,* or *thiocol,* $C_6H_3.OH.OCH_3.SO_3K$, occurs in white crystals which are soluble in about 7 parts of water and are insoluble in alcohol and ether. Like guaiacol, it acts as a sedative expectorant and it has the advantage of being less irritating. Its *syrup* (p. 223) is recognized by the Formulary. *Dose.*—0.5 Gm. (8 grains).

RESORCINOL—Resorcinol
(Resorcin.—Resorcin)

$C_6H_6O_2$



Molecular weight, 110.05

Resorcinol, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of $C_6H_6O_2$.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, needle-shaped crystals or colorless powder; characteristic odor; sweetish, then bitter taste; turns pink on exposure to light and air; soluble in about 0.9 part of water and in about 0.7 part of alcohol; quite soluble in glycerin or ether, slightly soluble in chloroform; melts between 109° and 111° C. For details, see U.S.P., p. 320.

For *tests for identity* and for *impurity* (catechol), see U.S.P., p. 320.

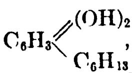
Remarks.—This body, metadihydroxybenzene, was first obtained by Hlasiwitz (1864), by fusing galbanum with potassa. It can be made in the same way from other gum resins, such, for example, as asafetida, and is now prepared synthetically by fusing metadisulfonbenzene, $C_6H_4(SO_3H)_2$, with sodium hydroxide.

Resorcinol occurs in white, feathery crystals, turning pinkish on exposure to air; soluble in water, alcohol, and ether. It is used chiefly externally in some forms of skin troubles because of its antiseptic action. Of late it has had considerable vogue as a remedy for dandruff. When taken internally, it possesses antipyretic properties.

Dose.—125 mg. (2 grains).

Orcein, the coloring matter of *cudbear* (p. 882) is a resorcin derivative.

Euresol, or resorcin monoacetate, has been recommended in dermatology and for use in hair tonics.

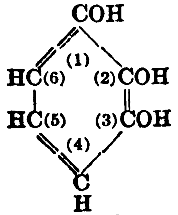


Hexylresorcinol, $C_6H_3\begin{cases}(OH)_2\\C_6H_{13}\end{cases}$, is a new urinary antiseptic which is claimed to have 45 times the antiseptic power of phenol. It is made by condensing resorcinol with normal caproic acid and then reducing the resulting ketone.

Hydroquinone is the paradioxy-derivative of benzene, and is obtained by oxidation of cinchonic acid. It is also obtained by hydrolysis of the glucoside arbutin (p. 721). It has practically no medicinal application, although very largely used in photography.

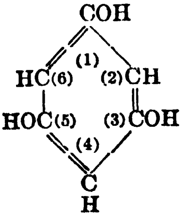
Triatomic phenols of benzene have the formula $C_6H_3(OH)_3$. As there were three diatomic phenols, so there are three bodies with the formula $C_6H_3(OH)_3$, and the graphic formulas of these are given below:

Vicinal trihydroxybenzene.



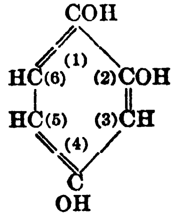
Pyrogallol.

Symmetric trihydroxybenzene.



Phlorogluoin.

Asymmetric trihydroxybenzene.



Oxyhydroquinone.

As will be noticed, in the vicinal form, the three hydroxyl groups are on adjoining carbon atoms; in the symmetric, the hydroxyl groups are each separated from the other by an interposed carbon atom; while in the asymmetric two are on adjoining carbon atoms and the other is separated by an interposed carbon atom.

In explaining it in the numeric way, in the vicinal the hydroxyl groups are on carbon atoms 1, 2, and 3; in the symmetric, they are on carbon atoms 1, 3, and 5, and in the asymmetric they are on carbon atoms 1, 2, and 4.

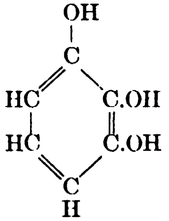
As the classification for the ortho-, meta-, and para-compounds applies to all di-derivatives of benzene, so also the classification of the vicinal, symmetric, and asymmetric applies to all tri-derivatives of benzene.

As noted above, the three tribasic phenols are called pyrogallol, phloroglucin, and oxyhydroquinone respectively.

PYROGALLOL—Pyrogallol

(**Pyrogall.**—Pyrogallic Acid)

$C_6H_6O_3$



Molecular weight, 126.05

Trihydroxybenzene, $C_6H_3(OH)_3$ 1:2:3.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White or nearly white laminæ or fine needles; bitter taste; turns grayish on exposure to light and air; soluble in about 1.7 parts of water, in about 1 part of alcohol and in about 1.1 parts of ether; melts between 130° and 133° C. For details, see U.S.P., p. 311.

For *tests for identity*, see U.S.P., p. 311.

Remarks.—Pyrogallol is what is commercially called *pyrogallic acid*, and was discovered by Scheele in 1786. It is made by strongly heating gallic acid, hence the name, pyrogallic acid; the prefix, *pyro*, as explained on p. 496, communicating the idea that the body has been produced by strong heat.

As will be explained under gallic acid, the heating of that product causes the loss of CO_2, with formation of the official pyroga'lol.

Pyrogallic acid is one of the most valuable reducing agents, having such strong affinity for oxygen that one volume of 2½ per cent alkaline solution absorbs 14 volumes of the gas, and for this reason it is used as an absorber in gas analysis. Its reducing action makes it valuable as a developer in photography, and it has of late been considerably used as one of the constituents of that class of hair dyes producing auburn or chestnut tints. These dyes consist of two solutions, one of either copper or nickel salts, and the other, pyrogallol, and when the hair is moistened with the solution of metallic salt and then treated with pyrogallol solution, a literal "copper plating" takes place.

Pyrogallol is used externally in skin troubles, but should be applied only under the direction of skilled physicians, as it is decidedly irritating in action.

Phloroglucin, $C_6H_3(OH)_3$ 1:3:5, is made by fusing kino with potassa or resorcin with soda. It is of no pharmaceutic value save as a test for wood paper (p. 703).

Oxyhydroquinone, $C_6H_3(OH)_3$ 1:2:4, is an oxidation product of quinine, but of no value either in medicine or pharmacy.

The amido derivatives of benzene are of almost equal importance to the hydroxyl derivatives, $C_6H_5NH_2$ being the well-known aniline.

Aniline was discovered as a distillation product from indigo by Helot in 1740; its presence in coal tar was demonstrated by Runge in 1824; while Fritsche investigating the coal-tar derivative in 1841, found it identical with the product from indigo and called it aniline, from the Portuguese name for indigo, "anil." The chemistry of the subject was not made perfectly clear until Hoffman's investigations of 1843, and the further researches of that chemist gave rise to our present dyestuff industry, with its enormous capital and its far-reaching influence.

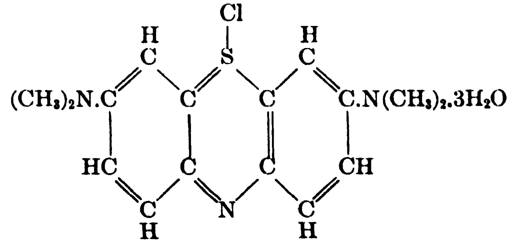
While the first aniline dyestuff, mauvein, was manufactured by Perkin in 1856, it was not until 1864 that the manufacture of aniline reached a commercial basis, and in that year the first aniline factory was established. While aniline itself is a constituent of coal tar, it has been found simpler to convert the benzene distillate of coal tar into the body by first changing same into nitrobenzene, $C_6H_5NO_2$, and reducing this to aniline, $C_6H_5NH_2$, by treating with hydrochloric acid and iron filings. The product of the reduction is then distilled with steam and purified by repeated distillation if necessary.

Aniline is a straw-colored liquid possessing a peculiar aromatic odor, somewhat similar to benzene; soluble in 31 parts of water and is neutral to litmus paper. It possesses valuable solvent properties—dissolving indigo, for instance. Its reactions are manifold, they leading to that exceedingly valuable class of compounds, the dye-stuffs, which at present have assumed such proportions as to make their study a science in itself, and far beyond the scope of this work.

Aniline dyes (so called) are not all simple derivatives of aniline. In fact, among the thousands of these dyes that are now so important a factor in the world's commerce, but few of them are really obtained directly from aniline. A discussion of these dyes is beyond the limits of this book but there are a few that must be discussed because of their pharmaceutic significance and all of these will be considered in this chapter.

METHYLTHIONINÆ CHLORIDUM—Methylthionine Chloride

(**Methylthionin. Chlor.**—Methylene Blue)



$C_{16}H_{18}N_3ClS.3H_2O$. **Molecular weight, 373.73**

Methylthionine Chloride, when dried to constant weight at 110° C., contains not less than 98.5 per cent of $C_{16}H_{18}N_3ClS$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Dark-green crystalline powder or prismatic crystals with bronzelike luster; soluble in water, alcohol and chloroform, forming blue solutions; aqueous solution lessened in color by addition of hydrochloric acid, and is turned purple by sodium hydroxide with eventual precipitation; zinc and diluted sulfuric acid reduce it to a colorless compound. For details, see U.S.P., p. 235.

For *tests for identity* and for *impurities* (dextrin, arsenic and zinc), see U.S.P., p. 235.

Remarks.—The manufacture of methylene blue opens up the complex question of the synthesis of aniline dyes. Aniline (Formula I) can be converted into paraphenylenediamine (Formula II), and this in turn can be methylated to dimethylparaphenylenediamine or para-aminodimethyl aniline (Formula III). When this substance is treated with hydrogen sulfide and ferric chloride, 2 molecules condense and add sulfur forming 1 molecule of methylene blue (Formula V).

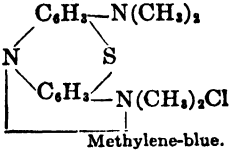
FORMULA I.
$C_6H_5NH_2$
Aniline.

FORMULA II.
$C_6H_4(NH_2)_2$
Paraphenylenediamine.

FORMULA III.
$H_2N—C_6H_4—N(CH_3)_2$
Dimethylparaphenylenediamine.

FORMULA IV.
$H_2N\ C_6H_4N(CH_3)_2$
$HHNC_6H_4N(CH_3)_2$
Condensation of dimethylparaphenylenediamine (ammonia splits off).

FORMULA V.



Methylene-blue.

It will be noted that this structural formula does not exactly coincide with the "official" formula given above. Here is another case "where the doctors disagree."

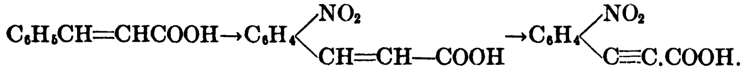
The commercial methylene blue is a double salt of the pure dye with zinc chloride, hence must not be used. This explains the test for the presence of zinc as given in the Pharmacopœia.

Methylene blue is used as an antiseptic in gonorrhea. It is very disagreeable to handle, because it stains everything with which it comes in contact a tenacious blue, which washing in water or alcohol will eventually (although very slowly) remove.

Dose.—150 mg. (2½ grains).

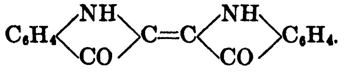
Indigo is an important dyestuff originally obtained from plants of the *Indigofera* species. It is now made synthetically upon a commercial scale by the reduction of ortho-nitro-phenyl-propiolic acid with glucose or with xanthogenates. The acid just mentioned is derived from cinnamic acid and in order to show the structure of indigo, the synthesis will be shown by formulæ below:

Cinnamic acid. Ortho-nitro-cinnamic acid. Ortho-nitro-phenyl-propiolic acid.



$$C_6H_5CH{=}CHCOOH \rightarrow C_6H_4\begin{cases} NO_2 \\ CH{=}CH—COOH \end{cases} \rightarrow C_6H_4\begin{cases} NO_2 \\ C{\equiv}C.COOH. \end{cases}$$

From two molecules of the latter acid by reduction is obtained one molecule of indigo; the graphic formula of which is:



$$C_6H_4\begin{matrix} NH \\ CO \end{matrix}C{=}C\begin{matrix} NH \\ CO \end{matrix}C_6H_4.$$

Indigo is now usually made by treatment of phenyl glycine, $C_6H_5NHCH_2COOH$, with sodamide, $NaNH_2$, followed by oxidation. It is also made from phthalimide, a body produced by treating phthalic anhydride (p. 814) with ammonia gas.

Sodii Indigotindisulfonas (U.S.P. X) was introduced merely because it is used to color *poison tablets of corrosive mercuric chloride* (p. 347). It is commonly called *indigo carmine* or *soluble indigo.* Indigo is insoluble in water and in order to make it water-soluble, it is first treated with concentrated sulfuric acid, producing indigotindisulfonic acid [$C_{16}H_8O_2N_2(SO_3H)_2$] and then this is converted into the less corrosive sodium salt, $C_{16}H_8O_2N_2(SO_3Na)_2$. Indigo carmine is marketed either in the form of a powder or paste.

OTHER ANILINE DYES

The following dyes are now used in modern medical treatment. *Acriflavine* or 3:6-diamino-methyl-acridine chloride; *proflavine* or 3:6-diamino-acridine sulfate; and *brilliant green* or tetra-ethyl-diamino-triphenyl methane were used during the World War in England with some success as antiseptics and their use obtains to this day. *Flavizid* and *rivenol* are two other dye-stuff antiseptics. All of these are complex bodies; all except brilliant green being derivatives of anthracene (p. 890).

ACRIFLAVINA—Acriflavine

(Acriflav.—Acriflavine Base, Neutral Acriflavine)

A mixture of 2, 8 diamino-10-methyl-acridinium chloride and 2, 8 diamino-acridine containing, when dried to constant weight at 100° C., not less than 13.3 per cent and not more than 15.8 per cent of Cl.

Storage.—Preserve in tightly-closed containers.

Summarized Description.

Brown-red, odorless powder; soluble in about 3 parts of water; incompletely soluble in alcohol; almost insoluble in ether, chloroform and fixed oils.

For *tests for identity,* for *impurities* (hydrochloride, arsenic) and for *assay,* see U.S.P., p. 33.

ACRIFLAVINÆ HYDROCHLORIDUM—Acriflavine Hydrochloride

(Acriflav. Hydrochlor.)

A mixture of the hydrochlorides of 2, 8 diamino-10-methyl-acridinium chloride and 2, 8 diamino-acridine containing, when dried to constant weight over sulfuric acid, not less than 23 and not more than 24.5 per cent of chlorine.

Storage.—Preserve in tightly-closed containers.

Summarized Description.

Orange-brown or red-brown, odorless, crystalline powder; soluble in about 3 parts of water and in alcohol; almost insoluble in ether and in chloroform.

For *tests for identity,* for *impurity* (arsenic) and for *assay,* see U.S.P., p. 34.

Remarks.—As mentioned above these two types of acridine dyes have been finally accorded pharmacopœial recognition. Both are used as antiseptics in the treatment of wounds, usually by irrigation. They are also used in gonorrhea and in nose and throat troubles.

Neutral acriflavine is also marketed in ½-grain enteric tablets, for use as an intestinal antiseptic. No dose is given for either type of acriflavine in U.S.P. XI.

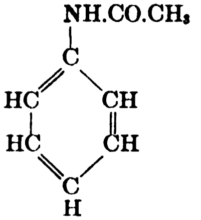
Methylrosanilinum (N.F. VI), or *gentian violet,* or *methyl violet,* or *crystal violet,* is a mixture of the methyl-pararosanilin chlorides. The hexamethyl compound predominates; the penta-methyl and the tetra-methyl compounds being unavoidable admixtures produced during the process of manufacture. Gentian violet (to employ its usual name) is used intravenously in sterile solution in streptococcic infections. The *solution* (p. 214) is recognized by N.F. VI.

Rubrum Scarlatinum (N.F. VI), or *Scarlet Red,* or *Biebrich scarlet R,* is tolyl-azo-betanaphthol, $CH_3C_6H_4N{=}N{-}C_6H_3(CH_3)N{=}N{-}C_{10}H_6OH$. It has been used rather extensively during the past few years for promoting the growth of epithelium in cases of burns. For this purpose an ointment consisting of 8 parts of scarlet red, 2 parts of eucalyptol and 90 parts of petrolatum is employed. The *ointment* (p. 372) is official in N.F. VI.

Amaranthum (N.F. VI), or *Amaranth Color,* has been introduced into the Formulary as a certified coal-tar food color. Its *solution* (p. 213) is used to color a few of the N.F. preparations.

ACETANILIDUM—Acetanilid

(Acetanil.)



C_8H_9ON Molecular weight, 135.08

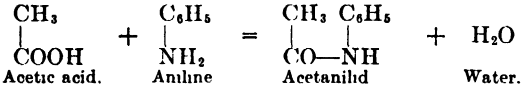
Monoacetylaniline.

Summarized Description.

Colorless, shining, micaceous, crystalline laminæ or crystalline powder; slightly burning taste; soluble in about 190 parts of water, in about 2.5 parts of alcohol and also soluble in chloroform, ether, acetone, benzene and glycerin; melts between 113° and 115° C. For details, see U.S.P., p. 10.

' For *tests for identity*, for *impurities* (carbonizable substances, aniline salts), see U.S.P., p. 10.

Remarks.—This body, formerly called *antifebrin*, represents aniline in which one of the hydrogen atoms is replaced by the acetyl (C_2H_3O) group. It is made by heating aniline with glacial acetic acid, the reaction being—



$$\underset{\text{Acetic acid.}}{\begin{matrix}CH_3\\|\\COOH\end{matrix}} + \underset{\text{Aniline}}{\begin{matrix}C_6H_5\\|\\NH_2\end{matrix}} = \underset{\text{Acetanilid}}{\begin{matrix}CH_3 & C_6H_5\\| & |\\CO & -NH\end{matrix}} + \underset{\text{Water.}}{H_2O}$$

Acetanilid, or *phenyl acetamide*, as it is sometimes called, occurs in white, shining laminae or in crystalline powder, sparingly soluble in alcohol, melting at about 114° C. It, like aniline, responds to the isonitrile reaction (p. 646).

Acetanilid is one of the most valuable antipyretics, although, like all the modern synthetics of this character, it should be used with caution. The indiscriminate use of these products has caused great harm, being particularly dangerous to persons with weak hearts. It is given in doses of 3 to 4 grains, either in powder or dissolved in brandy. An excess of acetanilid produces symptoms of coma and collapse, and the best antidote is copious drafts of brandy.

Dose.—200 mg. (3 grains).

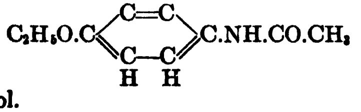
ACETANILID DERIVATIVES AND SUBSTITUTES

Exalgin is methyl acetanilid, or, more properly speaking, acettoluidide, and is made by heating toluidin $\left(C_6H_4\begin{matrix}CH_3\\NH_2\end{matrix}\right)$ with glacial acetic acid.

Antikamnia is a mixture of acetanilid, caffeine, tartaric acid, and sodium bicarbonate. A combination of this character is recognized in the National Formulary as Compound Powder of Acetanilid (p. 317).

ACETOPHENETIDINUM—Acetophenetidin

(Acetphen.—Acetphenetidinum U.S.P. X, Phenacetin)



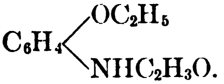
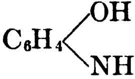
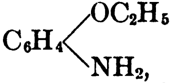
$C_{10}H_{13}O_2N$ Molecular weight, 179.11

Para-acetaminophenetol.

Summarized Description.

White, glistening, crystalline scales or fine crystalline powder; slightly bitter taste with numbing effect on the tongue, soluble in about 1300 parts of water, and in about 12 parts of alcohol; also soluble in chloroform and ether; melts between 134° and 135° C. For details, see U.S.P., p. 11.

For *tests for identity* and for *impurities* (carbonizable substances, acetanilid, paraphenetidin), see U.S.P., p. 12.

Remarks.—This body, commonly known as *phenacetin*, has the formula  $C_6H_4\begin{cases}OC_2H_5\\NHC_2H_3O.\end{cases}$ It represents acetanilid in which one of the hydrogen atoms is replaced by an OC_2H_5 group. Speaking more technically, it represents an ethyl-acetyl derivative of para-aminophenol,  $C_6H_4\begin{cases}OH\\NH_2\end{cases}$, and is made by the reduction of paranitrophenol, which, in turn, is prepared by treating phenol with cold diluted nitric acid. By treating para-aminophenol with ethyl iodide, p-phenetidin,  $C_6H_4\begin{cases}OC_2H_5\\NH_2,\end{cases}$ is produced, and by treating the latter with glacial acetic acid acetyl phenetidin or phenacetin results.

Konantz finds it cheaper to prepare acetphenetidin by chlorinating benzene, converting the resulting chlorobenzenes into chloro-nitrobenzenes and then producing successively paranitrophenol, paranitrophenetol, para-aminophenetol and finally para-acetphenetidin.

Phenacetin is a white powder that melts at 134° to 135° C. It is one of the most valuable antipyretics.

Phenacetin is sometimes contaminated with phenetidin. This latter is a dangerous irritant, hence such adulterated phenacetin should not be dispensed. Detection of same is easily accomplished by the pharmacopœial test given above.

Some unscrupulous dealers have adulterated phenacetin with acetanilid, but this can be easily detected by means of the melting point—phenacetin, 134° to 135°; acetanilid, 113° to 115°—or by the pharmacopœial chemical test given above.

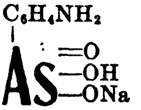
Dose.—300 mg. (5 grains).

CHEMOTHERAPY

During the past thirty years tremendous advances in medical practice have become possible through the scientific cooperation between the chemist and the physician. Such cooperation may be indicated by the word "chemotherapy." This term, while first used in connection with Ehrlich's work on salvarsan, is now used on a much broader field. In the bibliography found at the end of this chapter is recorded a number of thoughtful papers on the subject; so we will at this time proceed to a discussion of the arseno-organics and other metallo-organics.

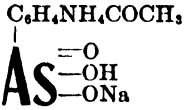
Arseno-organics.—During recent years, complex organic combinations containing arsenic have come into vogue as remedies for protozoal diseases, such as sleeping sickness, malaria, and syphilis. Among the chemicals thus employed we find *atoxyl*, or sodium arsenilate containing 3 molecules of water; *soamine*, or sodium arsenilate containing 5 molecules of water; *arsacetin*, or sodium acetyl arsenilate; *salvarsan* or "606," which is the hydrochloride of the sodium compound of dioxy-diamido-arseno-benzene; *neosalvarsan* which is the sodium combination of dioxy-diamino-arseno-benzene-methanal-sulfoxylate; and *stovarsol* or hydroxy-amino-benzene arsonic acid. The structural formulæ of the three that are of most importance are given below:

Sodium arsenilate.



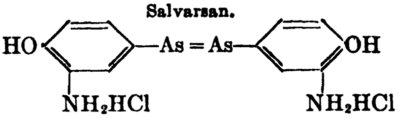
$$\mathrm{C_6H_4NH_2}-\mathrm{As}\begin{cases}=\mathrm{O}\\-\mathrm{OH}\\-\mathrm{ONa}\end{cases}$$

Arsacetin.



$$\mathrm{C_6H_4NH_4COCH_3}-\mathrm{As}\begin{cases}=\mathrm{O}\\-\mathrm{OH}\\-\mathrm{ONa}\end{cases}$$

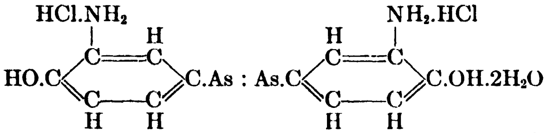
Salvarsan.



From these formulas, it will be seen that the first two are combinations of aniline and acetanilid with arsenic acid while "606" has as its basis a body $C_6H_5As{=}As{-}C_6H_5$ which is analogous to that largely used aniline derivative, azo-benzene, $C_6H_5N{=}N{-}C_6H_5$. Salvarsan is clearly the most important of the compounds just described. It is made by treating phenol with arsenic acid, thereby obtaining para-oxyphenyl arsenic acid. This is nitrated and the nitro-body is then reduced with sodium amalgam to aminophenyl arsenic acid. This substance on treatment with sodium hydroxide, sodium hydrosulfite and magnesium chloride yields diaminodihydroxyarsenobenzene, the hydrochloride of which is the commercial salvarsan.

ARSPHENAMINA—Arsphenamine

(**Arsphen.**—Diaminodihydroxyarsenobenzene Hydrochloride)



$C_{12}H_{14}O_2N_2Cl_2As_2.2H_2O$ Molecular weight, 474.89

Arsphenamine or 3,3′-diamino-4,4′-dihydroxyarsenobenzene dihydrochloride contains not less than 30 per cent of arsenic (As), and complies with the requirements of the National Institute of Health, United States Public Health Service.

Storage.—Preserve in sealed containers of colorless glass, from which the air has been excluded either by the production of a vacuum or by displacement with a non-oxidizing gas.

Summarized Description.

Light yellow powder; odorless or slight odor; oxidizes on standing, becoming darker and more toxic; soluble in water, alcohol and glycerin; slightly soluble in chloroform and ether. For details, see U.S.P., p. 73.

For *tests for identity*, for *impurity* (neoarsphenamine) and for *assay*, see U.S.P., p. 73.

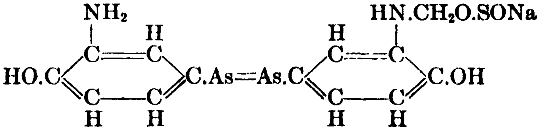
Remarks.—This is the *salvarsan* or "606" described above. It is a yellow, crystalline, hygroscopic powder, that is so unstable in air, that it has to be marketed in ampuls. Its introduction has opened a new field of activity for those pharmacists having the ability and inclination to prepare the chemical in an exactly neutral, sterile solution, sealed in an ampul (p. 988) ready for intravenous administration. There have been a number of methods suggested (see Bibliography), the simplest being as follows:

The weighed quantity of salvarsan (the commercial ampuls each contain a 0.6-Gm. dose) is triturated with 0.7 cc. of sterile normal sodium hydroxide solution for each 0.1 Gm. of salvarsan employed and then more of the alkaline solution is added, drop by drop, until complete solution occurs. This solution is then diluted with 100 to 250 cc. of sterile physiologic salt solution (0.9 per cent) after which it is filtered through a sterile filter. It is needless to say that the operation should be performed under absolutely aseptic conditions; that all the material and utensils should be sterile and that the room and the operator should be as near germ-free as possible.

Dose.—(Intravenous) 400 mg. (6 grains).

NEOARSPHENAMINA—Neoarsphenamine

(Neoarsphen.)



$C_{13}H_{13}O_4N_2SAs_2Na$ Molecular weight, 465.99

Neoarsphenamine consists chiefly of sodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene methanal sulfoxylate. It contains not less than 19 per cent and not more than 22 per cent of As and complies with the requirements of the National Institute of Health, United States Public Health Service.

Storage.—Preserve in sealed tubes of colorless glass, from which the air has been excluded either by the production of a vacuum or by displacement with a nonoxidizing gas, in a cool place, preferably not above 10° C.

Summarized Description.

Yellow powder; odorless or slight odor; oxidizes on standing, becoming darker and more toxic; very soluble in water; soluble in glycerin; sparingly soluble in alcohol; almost insoluble in dehydrated alcohol, acetone, chloroform and ether. For details, see U.S.P., p. 241.

For *tests for identity*, for *impurity* (arsphenamine) and for *assay*, see U.S.P., p. 241.

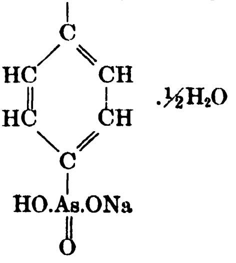
Remarks.—This product, formerly called *neosalvarsan,* has the advantage over salvarsan (or arsphenamine) of being more readily soluble in water.

Dose.—(Intravenous) 600 mg. (10 grains).

Silver Salvarsan is supposed to be a mixture of colloidal silver and sodium salvarsan. Ehrlich and Karrer, its discoverers, believe it to be a definite chemical in which the silver is attached to the arsenic of the salvarsan. It is claimed to be of value in general paralysis of the insane.

TRYPARSAMIDUM—Tryparsamide

(Tryparsam.)



$C_8H_{10}O_4N_2AsNa.\frac{1}{2}H_2O$ Molecular weight, 296.10

Sodium N-phenylglycinamide-p-arsonate, containing, when dried to constant weight at 110° C, not less than 25.1 per cent and not more than 25.5 per cent of arsenic (As).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White, odorless, crystalline powder; soluble in 2 parts of water, slightly soluble in alcohol, insoluble in ether and in chloroform.

For *tests for identity*, for *impurities* (arsonate, arsanilic acid, arsphenamine compounds) and for *assay*, see U.S.P., p. 414.

Remarks.—Tryparsamide is the sodium salt of N-phenylglycinamide-para-arsonic acid. Its formula is given above.

It is a product of the research of the Rockefeller Institute and is in the form of a white crystalline powder that is freely soluble in water. It is of particular value in African sleeping sickness and is used in certain types of syphilis. It should not be administered by mouth and is administered preferably intravenously.

Dose.—2 Gm. (30 grains).

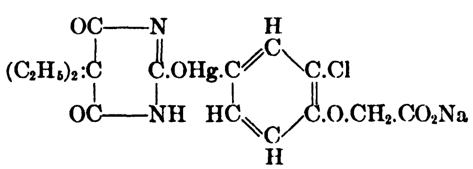
Sulfarsphenamine (N.N.R.) is the salt, disodium-diamino-dihydroxyarsenobenzene-dimethylenesulfonate, $NaOSO_2CH_2NHOH.C_6H_3As{=}AsCH_3OH.NHCH_2.O_2SONa$. It has the same actions and uses as neoarsphenamine, but is somewhat more stable and may be used by intramuscular injection. *Dose.*—0.4 to 0.5 Gm.

Stibno-organics.—A number of organic antimony compounds resembling the arseno-organics described above have been used recently in tropical diseases. Among these is *stibacetin* or para-acetylamino-phenyl-stibinate, $CH_3CONHC_6H_4SbO(OH)_2$.

Mercuro-organics.—A large number of organic mercury compounds are now enjoying a vogue in medicine. Of these the most important are *mercurochrome*-220, or dibrom-oxymercury fluorescein, *mercurophen*, sodium-oxymercuro-orthonitrophenolate, *merbaphen* (see below), *merthiolate* or sodium-ethyl-mercuri-thiosalicylate, and *mercurosal*, or disodium-hydroxy-mercuric salicylacetate. The first two are used as germicides, while mercurosal is intended to bring about the therapeutic effects of mercurials by intravenous injections.

MERBAPHENUM—Merbaphen

(Merbaphen.)



$C_{16}H_{16}O_6N_2ClHgNa$ Molecular weight, 591.20

The double salt of sodium-mercurichlorphenyl oxyacetate with diethyl-barbituric acid, containing, when dried to constant weight at 100° C., not less than 33 per cent and not more than 34.5 per cent of Hg.

Storage.—Preserve in well-closed containers.

Summarized Description.

White crystalline powder; soluble in cold water.

For *tests for identity* and for *assay*, see U.S.P., p. 232.

Remarks.—Merbaphen, or *novasurol*, is a mercurial antisyphilitic and diuretic that is administered either by hypodermic, intramuscular or intravenous injection. It contains from 33 to 34.5 per cent of mercury.

Dose.—By hypodermic injection, 0.15 Gm. (2½ grains).

BIBLIOGRAPHY

Benzene.—(History) Raubenheimer, Dr. Circ., 52, 1908, 421; Anon., Ch. and Dr., 88, 1916, 773; Anon., Jl. Soc. Ch. Ind., 42, 1923, 386; Pope, Jl. Soc. Ch. Ind., 44, 1925, 630; Partington, *ibid.*, 44, 1925, 358; Armstrong, *ibid.*, 48, 1929, 914; 50, 1931, 774 and Ph. Jl., 127, 1931, 253; Anon., Jl. Soc. Ch. Ind., 49, 1930, 434; Raw, *ibid.*, 50, 1931, 711. (Structure) Kekulé, A., 137, 1866, 129; Lifschitz, Zt. angew. Ch., 24, 1911, 1153; Willstätter and Waser, B., 44, 1911, 3423; Redgrove, Ch. News, 106, 1912, 224; Collie, C.A., 10, 1916, 2206; Vorländer, B., 52B, 1919, 263; Weinberg, B., 52B, 1919, 928; Shearer, Jl. Soc. Ch. Ind., 41, 1922, 562R.; Lely and others, C.A., 17, 1923, 1788 and 18, 1924, 1991; Huggins, Jl. Am. Ch. Soc., 45, 1923, 264 and 53, 1931, 1182; Haeckel, C.A., 24, 1930, 77. (Manufacture) Blucher, Midland Dr., 48, 1914, 291; Laurain and Deville, C.A., 5, 1911, 3902; Rittmann, C.A., 9, 1915, 2147; Egloff and Twomey, Ch. News, 114, 1916, 216; Downs, Jl. Soc. Ch. Ind., 50, 1932, 28 and 45. (Etymology) Raubenheimer, Ch. and Dr., 73, 1908, 144; Anon., Jl. Soc. Ch. Ind., 44, 1925, 56. (Properties) Meldrum, Ch. News, 113, 1916, 267; Menzies and Lacoss, C.A., 26, 1932, 5240. (Medical uses) Kuever, Dr. Circ., 59, 1915, 290. (Antidote) Nahum and Hoff, Science, Supp. 79, March 16, 1934, 9.

Oil of Mirbane.—Anon., Ch. and Dr., 107, 1927, 789.

Dichlorobenzenes.—Duckett, Jl. Soc. Ch. Ind., 34, 1915, 631; Anon., *ibid.*, 44, 1925, 56; Ehrlich, C.A., 25, 1931, 1401.

Benzene Derivatives.—(Nomenclature) Patterson, Jl. Am. Ch. Soc., 47, 1925, 543; Dobbin, Ch. and Dr., 110, 1929, 164 and 225.

Phenol.—(History) Runge (1834), through Thorpe, Dict., 4, 1913, 177. (Manufacture) Calvert, Ch. News, 17, 1868, 69. (Synthesis) Jayne, A.J.P., 63, 1891, 568; Ney, Met. Ch. Eng., 13, 1915, 686; Killeffer, Jl. Ind. Eng. Ch., 16, 1924, 1066; Rhodes and co-workers, *ibid.*, 19, 1927, 804. (Properties) Gibbs, Phillips, Jl. Sc., 1909, 361; Horiba, C.A., 9, 1915, 2346; Bennett, Ph. Jl., 106, 1921, 472; Mason, Jl. Soc. Ch. Ind., 49, 1930, 994; Schoorl, Ph. Weekbl., 67, 1930, 302; Ferrey, Ph. Jl., 126, 1931, 58. (Tests) Koppeschaar, Analyst, 11, 1886, 38; Gibbs, C.A., 21, 1927, 720. (Antiseptic action) Rideal and Walker, Ch. and Dr., 63, 1903, 975; England, Dr. Circ., 58, 1913, 204; Gawalowski, Merck's Rep., 20, 1911, 233; McClintic, Hyg. Lab. Bull. No. 82, 35. (Incompatibilities) Medley, Ph. Jl., 117, 1926, 149 and 209; Lum, *ibid.*, 122, 1929, 149. (Antidote) Clarke and Brown, Jl. A.M.A., 46, 1906, 782; Macht, Bull. Johns Hopkins Hosp., 26, 1915, 98; Wilbert, Jl. A.M.A., 67, 1916, 233.

Boulton's Solution.—Krantz and Carr, Jl. A.Ph.A., 18, 1929, 608.

Formolites.—Baekeland, Jl. Ind. Eng. Ch., 4, 1912, 737; 5, 1913, 506; 8, 1916, 186; 17, 1925, 225; Rowell, Jl. Soc. Ch. Ind., 46, 1927, 573 and 592; 48, 1929, 1158; Drummond, C.A., 22, 1928, 3307; Blumfeldt, C.A., 23, 1929, 5179; Morgan, Jl. Soc. Ch. Ind., 49, 1930, 245T; Nuttall, *ibid.*, 50, 1931, 299.

Anisol.—Merz, Ph. Zt., 60, 1915, 280.

Picric Acid.—(History) Anon., A.J.P., 6, 1834, 187; Marshall, Jl. Soc. Ch. Ind., 44, 1925, 4; Nierenstein, *ibid.*, 44, 1925, 117. (Manufacture) Hepp, B., 13, 1880, 2346; Ney, Met. Ch. Ind., 13, 1915, 3362. (Description) Malin, A., 138, 1866, 76. (Uses) Braun, A.Ph.A., 14, 1866, 189; Cassegrain, A.J.P., 92, 1920, 138.

Phenolsulfonic Acid.—Power and Raeuber, Ph. Rund., 7, 1889, 103.

Sozoiodol.—Larmuth, A.Ph.A., 37, 1889, 630.

Sozol.—Schaeges, A.Ph.A., 41, 1893, 531.

Aseptol.—Serrant, A.Ph.A., 34, 1886, 563.

Resorcinol.—(History) Hlasiwetz and Barth, A., 130, 1864, 354. (Manufacture) Power, A.J.P., 53, 1881, 221; Mühlhauser, Dingl. Poly. Jl., 263, 1887, 154; Phillips and Gibbs, Jl. Ind. Eng. Ch., 12, 1920, 857. (Properties) Bennett, Ph. Jl., 80, 1908, 758. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1155.

Hexylresorcinol.—Leonard and co-workers, Science, 62, 1925, 408 and 75, 1932, Supp 10; Jl. Soc. Ch. Ind., 45, 1926, 963B.

Euresol.—Anon., A.Ph.A., 47, 1899, 484 and 701.

Pyrocatechin.—(Structure) Petersen, B., 6, 1873, 308 and 7, 1874, 58. (Manufacture) Reinsch (1839), through Thorpe, Dict., 4, 1913, 179; Etti, A.Ph.A., 26, 1878, 55.

Guaiacol.—Leech, A.Ph.A., 37, 1889, 630; Carswell, Jl. A.Ph.A., 18, 1929, 995; Schwyzer, Ph. Zt., 75, 1930, 495, 509 and 518.

Guaiacol Carbonate.—Ehlert, Ph. Rev., 20, 1902, 211.

Pyrogallol.—(Manufacture) Liebig, A., 101, 1857, 47. (Properties) Weyl and Goth, B., 14, 1881, 2666. (Uses) Anon., Merck's Rep., 19, 1910, 42. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1155.

Aniline.—(History) Knecht, Jl. Soc. Ch. Ind., 17, 1898, 835; Parisel, Ch. News, 2, 1860, 77; Kopp, Ch. News, 2, 1860, 148; Anon., Nat. Dr., 40, 1910, 234; Schlenk, Zt. angew. Ch., 39, 1926, 757; Ed., Jl. Soc. Ch. Ind., 48, 1929, 1241.

Aniline Dyes.—(General) Levinstein, Jl. Soc. Ch. Ind., 43, 1924, 1029; Church, *ibid.*, 50, 1931, 391; Armstrong, *ibid.*, 50, 1931, 793.

Indigo.—Atkins, C.A., 15, 1921, 3399; Davis, Jl. Soc. Ch. Ind., 43, 1924, 266; King, Jl. Soc. Ch. Ind., 44, 1925, 135; Lowry, *ibid.*, 44, 1925, 230; Bailey, Ph. Era, 61, 1925, 655; Copenhaven, Jl. Ind. Eng. Ch., 22, 1930, 894; Ed., Jl. Soc. Ch. Ind., 51, 1932, 24.

Methylene Blue.—(Structure and manufacture) Bernthsen, A., 230, 1885, 137. (Tests) Raubenheimer, Am. Dr., 57, 1910, 369. (Uses) Ehrlich and Lippmann, A.Ph.A., 38, 1890, 689.

Scarlet Red.—Anon., Dr. Circ., 56, 1912, 201.

Acriflavine.—Browning, Am. Dr., 65, 1917, 400; Yearbook, A.Ph.A., 6, 1917, 453 and Nature, 109, 1922, 750; Bowlby, Ch. and Dr., 90, 1918, 14; Carlslow and Templeton, C.A., 12, 1918, 1567; Anon., Jl. A.M.A., 73, 1919, 1443; Davis and Ibarrell, Ch. and Dr., 91, 1919, 483; Fairbrother and Renshaw, Jl. Soc. Ch. Ind., 41, 1922, 134T; Volweiler, Jl. Ind. Ch., 15, 1923, 906; Collins and Stasiak, Jl. A.Ph.A., 18, 1929, 659; Marshall, Ph. Jl., 133, 1934, 80.

Proflavine.—Pearson, A.J.P., 90, 1918, 428; Bashford, Am. Dr., 66, 1918, 416; Hewlett, C.A., 12, 1918, 1567; Anon., Jl. A.M.A., 73, 1919, 1443; Fairbrother and Renshaw (see above).

Brilliant Green.—Browning, see above; Jones, Ph. Jl., 98, 1917, 337; Fairbrother and Renshaw, see above; Harvey, A.J.P., 96, 1924, 585.

Acetanilide.—(Manufacture) Gerhardt, A., 87, 1853, 164. (Uses) Cahn and Hepp, Am. Dr., 15, 1886, 209; Gane, Ph. Jl., 92, 1914, 698.

Exalgine.—Hepp and Hoff, B., 10, 1877, 328.

Antikamnia.—Hausmann, A.J.P., 63, 1891, 18.

Acetphenetidin.—(Structure) Anon., Ph. Jl., [3], 18, 1887, 264. (Manufacture) Konantz, Jl. A.Ph.A., 8, 1919, 284; Richardson, Jl. Soc. Ch. Ind., 45, 1926, 689B; Schwyzer, Ph. Zt., 75, 1930, 495, 509 and 518. (Properties) Reuter, A.J.P., 63, 1891, 375.

Chemotherapy.—Tiffaneau, C.A., 6, 1912, 654; White, Jl. Ind. Eng. Ch., 16, 1924, 1034; Loevenhart, *ibid.*, 18, 1926, 1268; Dyson, Ph. Jl., 116, 1926, 3, 32, 101, 170, 261 and 385; Carr, Jl. Soc. Ch. Ind., 46, 1927, 263T; King, *ibid.*, 47, 1928, 678; Barger, Ph. Jl., 123, 1929, 140; Hirschfelder and Wright, C.A., 24, 1930, 5873; Pyman, Jl. Soc. Ch. Ind., 49, 1930, 757.

Arseno-organics.—(General) Schweizer, Science, 32, 1910, 809; Humphrey, Merck's Rep., 18, 1909, 237; Martindale, Ch. and Dr., 77, 1910, 897; Launoy, Merck's Rep., 20, 1911, 78; Oesterle, Sch. Wsch. f. Ph. Ch., 51, 1913, 161; Morgan, Ph. Jl., 92, 1914, 567; Levaditi and others, C.A., 17, 1923, 1509; Giesma, Jl. Soc. Ch. Ind., 38, 1919, 598A.

Salvarsan.—(History) Ehrlich, B., 42, 1909, 17; Keenan, Am. Dr., 58, 1911, 103. (Manufacture) Turner, Am. Dr., 58, 1911, 5; Stieglitz, Jl. A.Ph.A., 7, 1918, 742; Lewis, Jl. Ind. Eng. Ch., 11, 1919, 141; Myers, Pract. Dr., 37, Sept., 1919, 39; Raiziss, Jl. Ind. Eng. Ch., 15, 1923, 413; Hirschfelder, *ibid.*, 15, 1923, 457. (Pharmacy) Fordyce, Am. Dr., 58, 1911, 55; Martindale, Ch. and Dr., 77, 1910, 897; Keenan, Am. Dr., 58, 1911, 105.

Neosalvarsan.—Upsher Smith, Jl. A.Ph.A., 1, 1912, 840.

Silver Salvarsan.—Ehrlich and Karrer, B., 48, 1915, 1634; Raiziss and Gavron, Jl. Pharmacol. Exp. Therap., 20, 1922, 163; Gray, Jl. Ch. Soc., 123, 1923, 635 and Jl. Soc. Ch. Ind., 44, 1925, 583; Binz and Bausch, B., 58B, 1925, 987.

Tryparsamide.—Jacobs and Heidelberger, Jl. A.C.S., 41, 1919, 1587 and Jl. Exp. Med., 30, 1919, 411; Vandercook, Merck's Rept., 40, 1931, 68; Anon., *ibid.*, 41, 1932, 56.

Antimony Organics.—Fargher, Jl. Soc. Ch. Ind., 39, 1920, 333R; Schmidt, C.A., 25, 1931, 557.

Mercury Organics.—Whitmore, Jl. Ind. Eng. Ch., 11, 1919, 1083 and 15, 1923, 417; Young, White and Swartz, Jl. A.M.A., 73, 1919, 1483; Schamberg, Kolmer and Raiziss, Jl. A.M.A., 68, 1917, 1458; Volweiler, Jl. Ind. Eng. Ch., 15, 1923, 907; Rowe, Jl. A.Ph.A., 12, 1923, 8 and 14, 1925, 317.

Merthiolate.—Powell and Jamieson, Pract. Dr., 51, Feb., 1933, 27.

Mercurochrome.—Scott and Hill, Jl. Urology, 14, 1925, 135 and C.A., 19, 1925, 2084; Rodriguez, Jl. A.M.A., 91, 1928, 708; Reddish and Drake, *ibid.*, 91, 1928, 712; Harvey, A.J.P., 102, 1930, 398; Foster, C.A., 24, 1920, 5072; Hynson, Westcott and Dunning, booklet, 1931, 1-32 (bibliography of 215 items); Phillips, Quart. Jl. Ph., 5, 1932, 1.

CHAPTER XLIV

TOLUENE COMPOUNDS

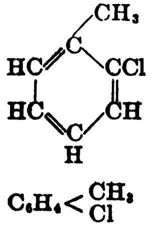
Toluene has the formula $C_6H_5CH_3$. It represents benzene in which one hydrogen is replaced by a methyl group. In this body, therefore, we have a combination of the ring and chain compounds, the methyl group possessing nearly all the reactions of the chain series of hydrocarbons, while the phenyl acts exactly as it did in benzene.

Toluene was first made by dry distillation of rosin by Pelletier and Walter in 1838. Deville (1841) obtained it by distillation of balsam of Tolu, and from this circumstance Berzelius named it toluol.

It can be easily made by several reactions; chief among these are, (1) the *Friedel Craft reaction*, in which benzene is treated with methyl chloride in the presence of aluminum chloride, and (2) by the *Fittig reaction* in which phenyl bromide is treated with methyl iodide in the presence of metallic sodium, this latter way being a modification of the Wuertz reaction mentioned on p. 639.

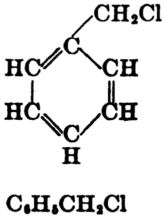
These two reactions are mentioned by name because affording means of the manufacture of any of the hydrocarbons of this series. Thus if ethyl chloride is substituted for the methyl chloride in the first reaction, or if ethyl iodide replaces methyl iodide in the second reaction, we would get ethyl benzene, $C_6H_5C_2H_5$.

Most commercial toluene, however, is obtained by the fractional distillation of coal tar, and is a colorless or amber-colored liquid, of aromatic odor, suggestive of benzene. It has a specific gravity 0.870, and boils at 110° C., and is insoluble in water, but freely soluble in alcohol. In its chemical behavior it resembles benzene, on one hand, and methane, on the other, and in the same way forms two distinct lines of hydrocarbon derivatives. Thus, the replacing of one hydrogen of the benzene group by the addition of chlorine gives rise to the compound known as monochlor-toluene, and this body is produced when chlorine is passed into cold toluene. On the other hand, if boiling toluene is treated with chlorine, the halogen replaces one of the hydrogens of the methyl group, forming the body called benzyl chloride. The structural difference between these two bodies is best shown by the graphic formulas given below. These two compounds are mentioned not because of their importance in themselves, but by reason of the possible forms when the respective chlorines are replaced by hydroxyls, in the first case a phenol (cresol) being formed, whereas the benzyl chloride yields benzyl alcohol, which possesses all the characteristics of an ordinary aliphatic alcohol.



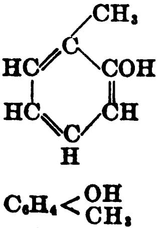
$C_6H_4<{}^{CH_3}_{Cl}$

Orthomonochlor-toluene.



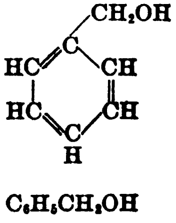
$C_6H_5CH_2Cl$

Benzylchloride.



$C_6H_4<{}^{OH}_{CH_3}$

Orthocresol.

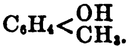
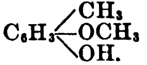
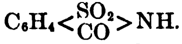
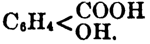
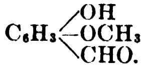
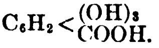


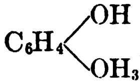
$C_6H_5CH_2OH$

Benzyl alcohol.

Under appropriate treatment of boiling toluene with chlorine, there is also yielded benzotrichloride, $C_6H_5CCl_3$, and benzal chloride, $C_6H_5CHCl_2$.

The toluene derivatives of pharmaceutic interest are:

Cresol, U.S.P.	 $C_6H_4<\substack{OH\\CH_3}.$
Creosol	 $C_6H_3\begin{cases}CH_3\\OCH_3\\OH.\end{cases}$
(Creosote, U.S.P. and creosote carbonate, U.S.P.)	
Benzyl alcohol	$C_6H_5CH_2OH.$
Benzaldehyde, U.S.P.	$C_6H_5CHO.$
(Oil bitter almond, U.S.P.).	
Benzoic acid, U.S.P.	$C_6H_5COOH.$
Ethyl aminobenzoate, U.S.P.	$C_6H_4\substack{NH_2\\C_6H_4COOC_2H_5.}$
Chloramine-T, U.S.P.	$C_6H_4\substack{CH_3\\SO_2NNaCl.3H_2O.}$
Dichloramine-T, U.S.P.	$C_6H_4\substack{CH_3\\SO_2NCl_2.}$
Saccharin, U.S.P.	 $C_6H_4<\substack{SO_2\\CO}>NH.$
Soluble saccharin, U.S.P.	$NaC_7H_4O_3NS + 2H_2O.$
Salicylic acid, U.S.P.	 $C_6H_4<\substack{COOH\\OH.}$
(Methyl salicylate, U.S.P.)	
Phenyl salicylate	$C_6H_4<\substack{OH\\COOC_6H_5.}$
Acetyl salicylic acid, U.S.P.	$C_6H_4\substack{OCOCH_3\\COOH}$
Vanillin, U.S.P.	 $C_6H_3\begin{cases}OH\\OCH_3\\CHO.\end{cases}$
Gallic acid, U.S.P. IX.	 $C_6H_2<\substack{(OH)_3\\COOH.}$
Tannic acid, U.S.P.	

The *cresols*,  $C_6H_4\begin{cases}OH\\OH_3\end{cases}$, are the monobasic phenols of toluene, and like all di-derivatives of benzene, are known in the *ortho-*, *meta-*, and *para-*forms.

CRESOL—Cresol

C_7H_8O. Molecular weight, 108.06

A mixture of isomeric cresols ($C_6H_4.CH_3.OH$) obtained from coal tar.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless or yellowish to brown-yellow or pinkish, highly refractive liquid; turns darker with age; phenol-like odor; soluble in about 50 parts of water; miscible with alcohol, ether, benzene, petroleum benzin or glycerin; soluble in solutions of fixed alkaline hydroxides; sp. gr. 1.030 to 1.038; at least 90 per cent distils between 195° and 205° C., exact details being given. For details, see U.S.P., p. 132.

For *tests for identity* and for *impurity* (hydrocarbons), see U.S.P., p. 132.

Manufacture.—In the manufacture of phenol from coal tar (see p. 772), the alkaline solution of the phenol fraction contains the cresols as well. When this alkaline solution is acidulated the cresols separate with the phenol and are separated by fractionation; they distilling between 195° and 205° C., while phenol distils at 188° C.

Remarks.—As mentioned in the official definition, commercial cresol (or *cresylic acid*, as it is frequently called) is a mixture of the three cresols mentioned above. It has been accorded pharmacopœial recognition because a constituent of the official, *compound solution of cresol.* It is sometimes used internally as an intestinal antiseptic.

Dose.—0.06 cc. (1 minim).

LIQUOR CRESOLIS SAPONATUS—Saponated Solution of Cresol

(Liq. Cresol. Sap.—Liquor Cresolis Compositus U.S.P. X, Compound Solution of Cresol)

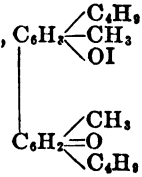
Storage.—Preserve in well-closed containers.

Condensed Recipe.

Mix 350 cc. linseed oil with 500 cc. cresol, add 14.52 Gm. 85 per cent potassium hydroxide and 37.05 Gm. 95 per cent sodium hydroxide and heat at 70° C. until saponification is complete. For details, see U.S.P., p. 206.

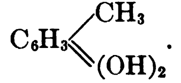
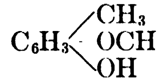
For *assay*, see U.S.P., p. 206.

Remarks.—This is a 50 per cent solution of cresol in an alkaline linseed oil soap solution, and is a product therapeutically similar to the proprietary alkaline solutions of coal-tar distillates. Like these, it is used as an antiseptic wash or douche.

Europhene N.N.R., 

$$\begin{array}{l} C_6H_2{<}\begin{matrix}C_4H_9\\ CH_3\\ OI\end{matrix} \\ | \\ C_6H_2{<}\begin{matrix}CH_3\\ =O\\ C_4H_9\end{matrix} \end{array}$$

is di-isobutyl-cresol-iodide. A comparison of the formula just given with the name shows how simple it is to express chemical structure in words. Europhene contains about 28 per cent of iodine and is used like aristol.

Homopyrocatechin, so named because of its similarity to pyrocatechin, is the diatomic phenol of toluene. Its formula is  $C_6H_3{<}\begin{matrix}CH_3\\ (OH)_2\end{matrix}$. Its methyl ester,  $C_6H_3{<}\begin{matrix}CH_3\\ OCH_3\\ OH\end{matrix}$, is known as *creosol,* and is of interest as a constituent of creosote.

CREOSOTUM—Creosote

(Cresot.—Creasote, Wood Creosote)

A mixture of phenols obtained from wood tar.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless or yellowish, highly refractive, inflammable oily liquid; penetrating smoky odor; burning caustic taste; should not become brown on exposure to light; slightly soluble in water; miscible with alcohol, ether, fixed or volatile oils; sp. gr. 1.076; distillation starts at 200° C., at least 90 per cent distils between 203° and 220° C.

For details, see U.S.P., p. 132.

For *tests for identity* and for *impurities* (phenol and "coal-tar creosote," hydrocarbons, bases), see U.S.P., p. 132.

Remarks.—This body was discovered by Reichenbach in 1830. The Pharmacopœia defines it "as a mixture of phenols obtained from wood tar."

The main constituents are guaiacol (described on p. 776), and creosol which has just been given.

Creosote is obtained either from pyroligneous acid, the empyreumatic liquid obtained by the destructive distillation of oak wood (p. 649), or from beechwood tar. As the last contains 25 per cent creosote, while pyroligneous acid yields only 1 per cent, the former source of creosote is preferred.

The separation of creosote from the tar is a laborious process. The tar is distilled, the half coming over first is allowed to stand, when it separates into three layers. The lowest layer is the one containing the creosote.

The creosote layer is separated from the others, and saturated with sodium carbonate to neutralize acetic acid present, and is then distilled. This distillate yields two layers, the lower of which contains the creosote, and this is purified by treatment with phosphoric acid. After neutralizing the acid with ammonia and washing the oil with water, it is again distilled, the distillate then consisting of creosote and *eupion;* the latter is a body named by Reichenbach, and consists chiefly of pentane. The creosote is freed from eupion by treatment with solution of potassa, which saponifies it, while eupion floats on top and can be separated. The saponified creosote is then treated with sulfuric acid, and the free creosote rectified by repeated distillations.

Creosote is a straw- to amber-colored liquid, possessing a characteristic tarry color, and somewhat burning taste. As already noted, a large amount of the creosote in commerce is nothing but an impure form of carbolic acid, and special emphasis should be laid on the fact that such "coal-tar creosote" should never be used for internal administration; nor is there any excuse for ignorantly dispensing same, inasmuch as the Pharmacopœia offers three distinct tests whereby the difference between creosote and phenol may be recognized: the collodion test and the glycerin-solubility test and the color produced with ferric chloride (pure violet blue with a solution of phenol; violet blue, then gray green and lastly muddy brown with a solution of creosote).

Creosote is a valuable antiseptic, its preservative action being due to the ease with which it coagulates albumin. This principle is employed in the so-called "smoking" of ham and other meats. The fresh meat is suspended in the vapors of burning wood, when the creosote of the vapors attacks the albumin on the outer surface of the ham, forming an impermeable and antiseptic layer. To secure best results in smoking, beechwood should be used, though this is seldom the case.

Dose.—0.25 cc. (4 minims).

Several preparations have been placed on the market under the name of "liquid smoke," and the like, and intended to be applied with a brush, consisting of various modifications of creosote or of crude pyroligneous acid, and this method of preserving meat is by no means so satisfactory as the old process of smoking.

CREOSOTI CARBONAS—Creosote Carbonate
(Creosot. Carb.)

Creosote Carbonate is a mixture of the carbonates of various constituents of creosote.

Summarized Description.

Clear, colorless or yellowish, viscid liquid; on chilling, guaiacol carbonate crystals separate; insoluble in water; soluble in alcohol, petroleum benzin or fixed oils; miscible with chloroform or benzene; sp. gr. not less than 1.145. For details, see U.S.P., p. 131.

For *tests for identity,* for *impurities* (creosote, "coal-tar creosote," hydrocarbons), see U.S.P., p. 131.

Remarks.—This official substance, called in trade *creosotal,* is prepared by passing phosgene into an alkaline solution of creosote. The resulting oily product is then purified by washing with weak alkali and then with water. It is a yellowish, viscid liquid, that is claimed to be a nonirritant substitute for creosote and is used like the latter, as a pulmonic and intestinal antiseptic.

Dose.—1 Gm. (15 grains).

CALCII CREOSOTAS—Calcium Creosotate
(Calc. Creosot.)

A mixture of the calcium compounds of the constituents of creosote. When dried to constant weight it yields, upon ignition, not less than 40 per cent and not more than 50 per cent of CaO.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Dark brown powder; empyreumatic odor; phenolic taste; partly soluble in water, but, on standing, calcium hydroxide and calcium carbonate precipitate. For details, see U.S.P., p. 98.

For *tests for identity* and for *assay*, see U.S.P., p. 98.

Remarks.—*Calcium creosotate*, or *calcreose* is a mixture containing in loose chemical combination, approximately equal weights of creosote and lime. It is claimed to be superior to creosote, since it does not readily produce gastric distress.

Dose.—0.5 Gm. (8 grains).

Benzyl Alcohol, $C_6H_5CH_2OH$, is the aromatic alcohol of toluene and is a constituent of balsam of Peru and balsam of tolu. It can be made by treating benzyl chloride with moist silver oxide or by treating benzaldehyde with potassium hydroxide.

It is a colorless liquid of faint aromatic odor, boiling between 201° and 206° C. and is soluble in 25 parts of water.

Benzyl alcohol has come into medical use through the pharmacological research of Macht, who finds that the benzyl group possesses marked anesthetic properties. (See p. 797.)

Benzyl alcohol, like all primary alcohols, oxidizes first to aldehyde and then to acid, and in this way differs markedly from the cresols mentioned above, these being phenols, resembling more closely either the tertiary or the secondary alcohols.

Benzaldehydum (U.S.P. X; N.F. VI), or *Benzaldehyde*, C_6H_5CHO, can be made by the oxidation of the benzyl alcohol just mentioned, or by treatment of benzyl chloride with milk of lime. It occurs in nature as the chief constituent of oil of bitter almond, It is used in perfumery, and rarely employed medicinally. *Dose.*—0.03 cc. (½ minim).

OLEUM AMYGDALÆ AMARÆ—Oil of Bitter Almond
(Ol. Amygd. Amar.—Bitter Almond Oil)

Oil of Bitter Almond is the volatile oil obtained from the dried ripe kernels (deprived of fixed oil) of *Amygdalus communis* Linné (Fam. *Rosaceæ*), or from other kernels containing amygdalin, by maceration with water and subsequent distillation with steam.

Oil of bitter almond contains not less than 95 per cent of benzaldehyde ($C_6H_5.CHO$), and not less than 2 per cent and not more than 4 per cent of hydrogen cyanide (HCN). Oil in which crystals have formed must not be dispensed.

Caution.—This oil is intended for medicinal use and neither it nor its solution should be used or sold for flavoring foods.

Storage.—Preserve in well-filled bottles, in a cool place and protected from light.

Summarized Description.

Clear, colorless or yellow, strongly refractive liquid; characteristic odor and taste; slightly soluble in water; soluble in alcohol and ether, also in 2 volumes of 70 per cent alcohol; sp. gr. 1.038 to 1.060; refractive index, 1.5428 to 1.5439; optically inactive or very slightly dextrorotatory. For details, see U.S.P., p. 247.

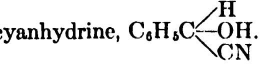
For *tests for identity,* for *impurities* (chlorinated products, nitrobenzene, heavy metals) and for *assay*, see U.S.P., p. 247.

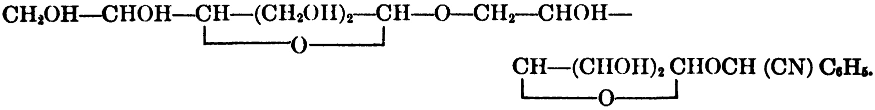
This is the volatile oil obtained from bitter almond by maceration with water and subsequent distillation.

Bitter almonds yield both fixed and volatile oil, and "sweet almond oil"—the expressed oil of almond—is obtained by expression from both kinds of almonds—bitter as well as sweet (p. 731).

Bitter almond in its dry form contains no volatile oil—no oil of bitter almond. To produce this, it is necessary to mash up the seed and add water, when a chemical reaction occurs between the amygdalin and emulsin present in the seed, one of the products of the reaction being oil of bitter almond.

Amygdalin belongs to the class of substances called glucosides (p. 713), which are bodies that on treatment with a diluted acid or ferment split into glucose and some other body. Emulsin is one of the unformed ferments explained on p. 952, hence a body that can break up amygdalin, as outlined above.

Feist has shown that the hydrolysis of amygdalin is not so simple as the reaction shown on page 713. The first step of the hydrolysis is the formation of one molecule of benzaldehyde-cyanhydrine,  $C_6H_5C\begin{matrix}\diagup H\\ —OH\\ \diagdown CN\end{matrix}$. This when treated with steam in the process of distillation breaks into benzaldehyde and hydrocyanic acid. Haworth and Leitch consider amygdalin as mandelonitrile-beta-maltoside and ascribe to it the formula



$$CH_2OH—CHOH—\underbrace{CH—(CH_2OH)_2—CH}_{O}—O—CH_2—CHOH—\underbrace{CH—(CHOH)_2\,CH}_{O}OCH\,(CN)\,C_6H_5.$$

When the amygdalin is split up by the emulsin, glucose, hydrocyanic acid, and oil of bitter almond are the three decomposition products, and only by the breaking up of the amygdalin is the oil developed. In the dry seed the amygdalin and emulsin rest quietly side by side, just as do the sodium bicarbonate and tartaric acid in dry effervescent salts, such as granular magnesium citrate. As soon as the water is added, just as the effervescent salts show energetic chemical action, even so, though marked only by the development of the bitter almond odor, does the emulsin react with the amygdalin.

In obtaining the bitter almond oil the fixed oil is separated by expression. The press cake is then mixed with water at 50° C. for about a day and then distilled. This results in the hydrolysis of the amygdalin under the influence of the enzyme emulsin, as just explained. When using the enzyme, great care must be exercised to prevent too great heat, as that causes decomposition of the enzyme and its subsequent inactivity. This statement is worth bearing in mind, as there has arisen the erroneous impression that the reason why cold water is used in the wild-cherry preparations is to prevent the evaporation of the hydrocyanic acid. This is only partly true, the real object of avoiding hot water being to prevent decomposition of the enzyme employed. From the volatile oil of bitter almond the hydrocyanic acid can be removed by treatment with ferrous sulfate and milk of lime and redistillation of the product with steam. This, however, is not done in the manufacture of the pharmaceutic oil, the Pharmacopœia specifying that same shall contain 2 to 4 per cent hydrocyanic acid, and this fact gives us a means of distinction between the synthetic benzaldehyde (which is free from hydrocyanic acid) and the natural oil of bitter almond. A very large quantity of such oil of bitter almond on the market represents synthetic benzaldehyde, and can be detected as mentioned above. Note, in the pharmacopœial description given above, that the crystals forming in bottles of the oil consist of benzoic acid.

Do not confound synthetic oil of bitter almond—benzaldehyde—with the so-called "artificial oil of bitter almond" or *oil of mirbane.* This has nothing to do with the almond; being $C_6H_5NO_2$, nitrobenzene. Its unfortunate synonym is due to the fact that its odor suggests that of bitter almond.

Dose.—0.03 cc. (½ minim).

Amygdala Amara (U.S.P. VIII), or *Bitter Almond,* is the ripe seed of *Prunus amygdalus* Stokes, var. *amara* De Candolle (Fam. *Rosaceæ*). It contains fixed oil, 35 to 62 per cent; amygdalin, 2 to 3 per cent; emulsin; asparagin and proteid (amandin).

The formation of the volatile oil, which does not exist in the dry seeds, but which is formed by the action of the emulsin on amygdalin, has been fully described just above. It acts as a sedative and is used largely as a flavor.

PRUNUS VIRGINIANA—Wild Cherry

(Prun. Virg.—Wild Black Cherry Bark)

Wild Cherry is the stem bark of *Prunus serotina* Ehrhart (Fam. *Rosaceæ*), collected in autumn and carefully dried. Borke, if present, should be removed.

Storage.—Preserve in tightly-closed containers, protected from light and moisture.

Constituents.—Mandelonitrile glucoside (which is similar to, but not identical with, amygdalin); an enzyme, similar to emulsin; volatile oil; two resins; benzoic, trimethyl-gallic and paracoumaric acids; sugar; tannin, phlobaphene and a fluorescent substance.

Remarks.—The dry bark contains neither oil nor hydrocyanic acid, but, like bitter almond, these principles are produced when the bark is moistened, and, therefore, constitute the medicinal activity of the drug. A simple test for wild cherry is that it is the only official bark which, when chewed, gives the odor of hydrocyanic acid (or of bitter almond). The ferment emulsin is rendered inactive when treated with hot water, and no oil nor hydrocyanic acid will be developed in wild cherry when so heated; hence all official preparations of the bark, including the infusion, are made with cold solvents. The *syrup* (p. 220) is official.

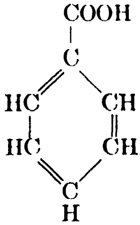
Medical Properties.—Tonic, mild sedative (for coughs).

Dose.—(U.S.P. X) 2 Gm. (30 grains).

ACIDUM BENZOICUM—Benzoic Acid

(Acid. Benz.)

$C_7H_6O_2$



Molecular weight, 122.05

Benzoic Acid, dried at 100° C. for two hours, contains not less than 99.3 per cent of $HC_7H_5O_2$.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Lustrous scales or friable needles; nearly odorless (the synthetic) or smelling like benzoin (the natural); pungent acid taste; somewhat volatile at moderately warm temperatures; volatilized by steam; soluble in about 275 parts of water and in about 1.8 parts of alcohol; also soluble in ether, chloroform, carbon disulfide, benzene, carbon tetrachloride, oil of turpentine, fixed and volatile oils; melts between 120° and 122° C. For details, see U.S.P., p. 17.

For *tests for identity,* for *impurities* (carbonizable substances, cinnamic acid, chlorinated compounds) and for *assay,* see U.S.P., p. 17.

Remarks.—Benzoic acid represents the final oxidation product of benzyl alcohol, this yielding benzaldehyde, and it in turn yielding benzoic acid.

$$\underset{\text{Benzyl alcohol.}}{C_6H_5CH_2OH} \rightarrow \underset{\text{Benzaldehyde.}}{C_6H_5CHO} \rightarrow \underset{\text{Benzoic acid.}}{C_6H_5COOH.}$$

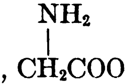
Benzoic acid was discovered by Vigenère in 1608 in benzoin, hence the name. Scheele in 1785 discovered it was a constituent of the urine, and Liebig and Woehler in 1832 proved its chemical composition. As mentioned above, benzoic acid is a normal constituent of benzoin, and is also an important constituent of balsams; balsams being oleoresins containing benzoic and cinnamic acids.

Benzoic acid can be made from benzene by converting same first into phenyl chloride, C_6H_5Cl, changing this to benzonitril, C_6H_5CN, and treating this with potassium hydroxide, when the potassium benzoate is formed.

As mentioned above, it is also made by the oxidation of either benzyl alcohol or benzaldehyde. Commercial benzoic acid, however, is usually manufactured by one of the four following methods:

(*a*) *Sublimation of benzoin,* as described fully on p. 126.

(*b*) *From Hippuric Acid.*—This body is a constituent of the urine of cattle, and is benzoyl glycocoll, $C_6H_5CONHCH_2COOH$.

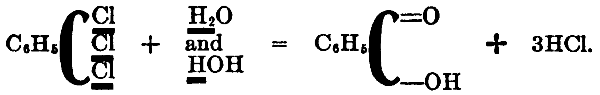


On boiling this substance with hydrochloric acid it splits into glycocoll (amino-acetic acid), $\overset{\overset{NH_2}{|}}{C}H_2COOH$, and benzoic acid.

The benzoic acid thus produced is usually mixed with benzoin and resublimed, and when fresh, is an acceptable preparation. In older samples the origin can be readily detected by the odor of stale urine. The benzoic acid of this source was formerly used in considerable quantities under the name of *German benzoic acid,* but at the present time the process has been largely supplanted by a third method of manufacture.

(*c*) *From Toluene.*—A comparison of the formulas of toluene, $C_6H_5CH_3$, and of benzoic acid, C_6H_5COOH, will show that the difference between them is slight; benzoic acid has 2 atoms of oxygen more and 2 atoms of hydrogen less, and, therefore, it should be easily prepared by oxidation.

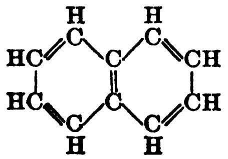
This, however, is not wholly the case, the reaction being rather indirect. Toluol is treated with chlorine, changing it, $C_6H_5CH_3$, into $C_6H_5CCl_3$, and this, when boiled with water, is converted into benzoic and hydrochloric acids, by the following reaction:



$$C_6H_5\left\{\begin{matrix}Cl\\Cl\\Cl\end{matrix}\right. + \begin{matrix}H_2O\\\text{and}\\HOH\end{matrix} = C_6H_5\left\{\begin{matrix}=O\\ \\-OH\end{matrix}\right. + 3HCl.$$

(*d*) *Process of Manufacture from Naphthalene.*—This body is $C_{10}H_8$, or, graphically, as expressed in Formula I below, and on oxidation with nitric acid, it yields phthalic acid, $C_6H_4(COOH)_2$, which is graphically expressed in Formula II.

FORMULA I



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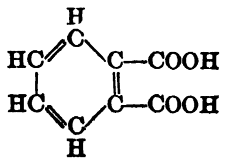
FORMULA II



Phthalic acid, on treatment with calcium hydroxide, loses one CO_2 group, and is converted into benzoic acid, C_6H_5COOH, or rather into its calcium salt.

Benzoic acid is used as an antiseptic and employed medicinally chiefly in the form of metallic benzoates.

Dose.—1 Gm. (15 grains).

BENZOIC ACID DERIVATIVES

The researches of Macht have shown the anesthetic qualities of the benzyl group and as a result a number of benzyl compounds are now largely used in medicine. Among these may be cited:

Benzyl Alcohol, $C_6H_5CH_2OH$ (see p. 793).

Benzyl Benzoate, $C_6H_5CH_2C_7H_5O_2$, is made by treating benzyl alcohol, $C_6H_5CH_2OH$, with benzoic acid, $HC_6H_5O_2$, in the presence of a dehydrator or catalyst. It is a liquid boiling at 300° to 325° C. and while insoluble in water it dissolves in all proportions of alcohol.

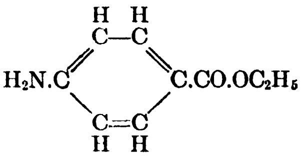
In his study of the two alkaloids of opium, morphine and papaverine, Macht found that the characteristic action of the latter alkaloid was due to the benzyl group that it contained. This led him to a study of benzyl compounds and to the discovery of antispasmodic and local anesthetic action of benzyl alcohol (see p. 793) and of benzyl benzoate.

Aminobenzoic Acids, $C_6H_4{}^{NH_2}_{COOH}$, occur in the three forms, ortho, meta and para (p. 775). They are made by the reduction of the nitrobenzoic acids. The esters of ortho-aminobenzoic acid (anthranilic acid) are found in the natural perfume of certain flowers and fruits (p. 835). A number of derivatives of para-aminobenzoic acid are used as local anesthetics and of these, two are now official, *procaine* (p. 913) and *benzocaine* (see below).

ÆTHYLIS AMINOBENZOAS—Ethyl Aminobenzoate

(Æthyl. Aminobenz.—Benzocaine)

$C_9H_{11}O_2N$



Molecular weight, 165.09

Storage.—Preserve in well-closed containers.

Summarized Description.

White or colorless crystals or white powder; odorless; soluble in about 2500 parts of water and about 4 parts of alcohol; also soluble in chloroform, ether, fixed oils and in dilute acids; melts between 88° and 90° C. For details, see U.S.P., p. 40.

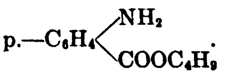
For *tests for identity* and for *impurities* (carbonizable substances, free acid, chloride, heavy metals, arsenic), see U.S.P., p. 41.

Remarks.—This official, originally introduced under the trade-marked named *anesthesin*, has the formula given above.

It occurs as a white crystalline powder melting at about 90° C. and is so sparingly soluble in water that it is unsuitable for hypodermic injections. The sparing solubility, however, makes it safer since more slowly absorbed and it is therefore of service as a local application, in ointment form for painful wounds and ulcers.

Dose.—300 mg. (5 grains).

Butesin (N.N.R.) is the normal butyl ester of para-aminobenzoic acid:

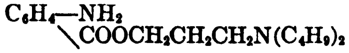


$$p.\text{—}C_6H_4{<}^{NH_2}_{COOC_4H_9}.$$

It is used as a difficultly soluble local anesthetic; its action being similar to benzocaine.

Dose.—300 mg.

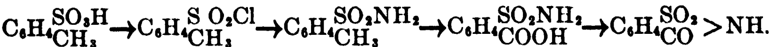
Butyn (N.N.R.) is the sulfate of para-amino-benzoyl-gamma-di-normal-butylamino-propanol.



$$C_6H_4{\begin{smallmatrix}-NH_2\\ \diagdown COOCH_2CH_2CH_2N(C_4H_9)_2\end{smallmatrix}}$$

It is a colorless and odorless solid, that is soluble in less than its own weight of water. It is used as an anesthetic in eye troubles in a 2 per cent solution.

Sulfobenzoic acid, $C_6H_4{\begin{smallmatrix}SO_3H\\ COOH\end{smallmatrix}}$, made by treating benzoic acid with sulfuric acid, is mentioned because of its imido-derivative, *saccharin*, $C_6H_4{\begin{smallmatrix}SO_2\\ CO\end{smallmatrix}}NH$, which was discovered by Remsen and Fahlberg in 1879. Its synthesis can best be expressed by successive products of the reaction:



$$C_6H_4{\begin{smallmatrix}SO_3H\\ CH_3\end{smallmatrix}} \rightarrow C_6H_4{\begin{smallmatrix}SO_2Cl\\ CH_3\end{smallmatrix}} \rightarrow C_6H_4{\begin{smallmatrix}SO_2NH_2\\ CH_3\end{smallmatrix}} \rightarrow C_6H_4{\begin{smallmatrix}SO_2NH_2\\ COOH\end{smallmatrix}} \rightarrow C_6H_4{\begin{smallmatrix}SO_2\\ CO\end{smallmatrix}} > NH.$$

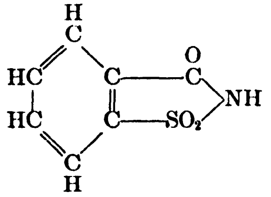
(Sulpho-toluene) Ortho-toluol-sulphochloride. Ortho-toluol-sulphamide. (Ortho-sulphamide benzoic acid). (Saccharin).

Toluene, when treated with sulfur trioxide, yields sulfotoluene, $C_6H_4{\begin{smallmatrix}SO_3H\\ CH_3\end{smallmatrix}}$. This yields successively the products given above, the end-product being

SACCHARINUM—Saccharin

(**Saccharin.**—Glusidum U.S.P. X, Gluside, Benzosulfinidum)

$C_7H_5O_3NS$



Molecular weight, 183.11

Orthosulfobenzimide.

Summarized Description.

White crystals, or white crystalline powder; odorless or faintly aromatic; 300 to 500 times sweeter than sucrose (sugar); soluble in about 290 parts of water and in about 25 parts of alcohol; also soluble in chloroform and ether and in some alkaline solutions; melts not below 222° C.

For details, see U.S.P., p. 322.

For *tests for identity* and for *impurities* (carbonizable substances, glucose, lactose, benzoic and salicylic acids, ammonium compounds), see U.S.P., p. 322.

Remarks.—Saccharin is in the form of white powder, sparingly soluble in water, and possessing a taste that has been graphically described as being "so sweet that it is bitter" (being 300 to 500 times sweeter than sugar), and in order to obtain its full sweetening power it is necessary that it be diluted. Administered as a sweetener, it is usually combined with alkali, such as sodium bicarbonate, and the saccharin tablets intended for use by diabetic patients in place of sugar are combined with the required quantity of alkali before compression. The addition of alkali is in order to render them more soluble.

As noted in the summarized description just given, saccharin is only sparingly soluble in water. The sodium compound, on the other hand, is very soluble, although not so powerful an antiseptic.

Saccharin is by no means a harmless agent, and its indiscriminate use as a sweetener should be deprecated. For diabetic patients it is a boon, but, on the other hand, for sweetening foods in order to spare the cost of the sugar its use should be strongly condemned.

It is of interest to note that saccharin possesses valuable antiseptic properties, the researches of Miller showing that saccharin ranked in activity next to bichloride of mercury as an agent for destroying the bacteria of the mouth. •

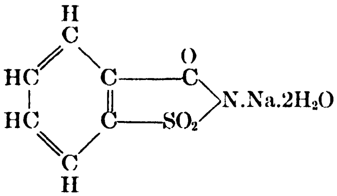
Professor Miller devised a saccharin mouth wash containing saccharin, an astringent substance like krameria, blended with aromatics, and products similar to this are among the most popular of the modern mouthwash preparations.

Dose.—30 mg. (½ grain) has about the sweetness of "a lump of sugar."

SACCHARINUM SOLUBILE—Soluble Saccharin

(**Saccharin. Sol.**—Glusidum Solubile U.S.P. X, Soluble Gluside, Sodii Benzosulfinidum)

$C_7H_4O_3NSNa.2H_2O$



Molecular weight, 241.13

The sodium salt of orthosulfobenzimide.

Summarized Description.

Colorless, rhombic crystals or white crystalline powder; odorless or faintly aromatic, intensely sweet taste; soluble in about 1.2 parts of water and in about 40 parts of alcohol. For details, see U.S.P., p. 323.

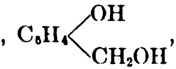
For *tests for identity* and for *impurities*, see Saccharin.

Remarks.—This official substance is the soluble form of saccharin described above.

Dose.—(Same as saccharin.)

SALICYL COMPOUNDS

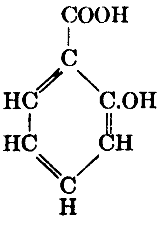
Among the salicyl compounds should be cited:

Saligenin or orthosalicylalcohol,  $C_6H_4\begin{cases}OH\\CH_2OH\end{cases}$, which is the hydrolysis product of salicin (p. 717). This is used in 12 per cent solution by Hirschfelder, who has prepared a number of saligenin derivatives.

ACIDUM SALICYLICUM—Salicylic Acid

(**Acid. Salicyl.**—Orthohydroxybenzoic Acid)

$C_7H_6O_3$



Molecular weight, 138.05

Salicylic acid, dried at 100° C. for two hours, contains not less than 99.5 per cent of $HC_7H_5O_3$.

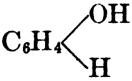
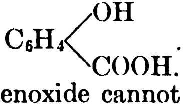
Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Fine prismatic needles or bulky crystalline powder; sweetish, then acrid taste; synthetic is white and odorless; natural is yellowish or pinkish and smells like gaultheria; soluble in about 460 parts of water and in about 2.2 parts of alcohol; also soluble in chloroform, ether, acetone, benzene and oil of turpentine; melts between 157° and 159° C. For details, see U.S.P., p. 26.

For *tests for identity*, for *impurities* (phenol, coloring matter, carbonizable substances, chloride, sulfate) and for *assay*, see U.S.P., p. 26.

Remarks.—This body, *ortho-hydroxybenzoic acid*, was discovered and named by Piria in 1839 as an oxidation product of salicin. It occurs naturally in several of the volatile oils, notably that of wintergreen and sweet birch. The synthesis of salicylic acid has been accomplished in several ways. One is by fusing salicin with potassium hydroxide. It can also be made by treating orthocresol with potassa, but its commercial manufacture is by treatment of sodium phenoxide or carbolate, with carbon dioxide, this being the celebrated *Kolbe process*.

This can be best explained as the insertion of a molecule of CO_2 into a molecule of phenol. Phenol is C_6H_5OH, or it can be expressed as  $C_6H_4\genfrac{<}{}{0pt}{}{OH}{H}$; treat this with CO_2, and we get salicylic acid,  $C_6H_4\genfrac{<}{}{0pt}{}{OH}{COOH}$.

It is interesting to note that in this case potassium phenoxide cannot be used for the sodium phenoxide. If the potassium phenoxide is used, instead of getting ortho-hydroxybenzoic acid, we obtain the para-hydroxybenzoic acid.

Salicylic acid occurs in fine white needles or light crystalline powder. It gives a very characteristic and delicate reaction with ferric chloride, the latter agent giving a distinct red tint in an aqueous solution of 1 part salicylic acid to 400,000 parts of water, or, roughly speaking, 1 grain dissolved in 7 gallons of water will give distinct reaction with ferric chloride. More concentrated solutions of salicylic acid or salicylates give a deep purple precipitate with ferric chloride.

Salicylic acid is a valuable antipyretic, antirheumatic, and antiseptic.

Incompatibilities.—See prescription No. 48 in Chapter LIX.

Dose.—(U.S.P. X) 750 mg. (12 grains).

Para-oxybenzoic Acid has a methyl ester, *nipagin*, which is largely used in Germany as a preservative for pharmaceuticals and cosmetics.

Several derivatives of salicylic acid are official: the salicylates of the metals, sodium, ammonium, strontium, mercury and bismuth; of the alkaloid, physostigmine; and the esters, methyl salicylate and phenyl salicylate.

METHYLIS SALICYLAS—Methyl Salicylate

(Methyl. Salicyl.—Oil of Gaultheria, Oil of Wintergreen, Oil of Betula, Oil of Sweet Birch)

$C_8H_8O_3$. Molecular weight, 152.06

Methyl Salicylate is produced synthetically or is obtained by distillation with steam from the leaves of *Gaultheria procumbens* Linné (Fam. *Ericaceæ*) or from the bark of *Betula lenta* Linné (Fam. *Betulaceæ*).

Methyl Salicylate must be labeled to indicate whether it was made synthetically or distilled from either of the plants mentioned above. It contains not less than 98 per cent of $C_6H_4(OH)CO_2CH_3$.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless, yellowish or reddish liquid; odor of gaultheria; sparingly soluble in water; miscible with alcohol and with glacial acetic acid; soluble in 7 volumes of 70 per cent alcohol with but little cloudiness; sp. gr. 1.180 to 1.185 (synthetic), 1.176 to 1.182 (natural); boils between 219° and 224° C. For details, see U.S.P., p. 234.

For *tests for identity*, for *impurities* (free acid, heavy metals) and for *assay*, see U.S.P., p. 234.

Remarks.—The present Pharmacopœia recognizes under the title *methylis salicylas* the three commercial varieties of this chemical; the synthetic form and the two natural oils, that of wintergreen and of sweet birch. Synthetic methyl salicylate is made by treating methyl alcohol with salicylic acid in the presence of sulfuric acid, as shown by the following equation:

$$CH_3OH + HC_7H_5O_3 = CH_3C_7H_5O_2 + H_2O.$$

In this case, as in making all esters, the sulfuric acid acts as either a dehydrator or as a catalyst. While both oil of sweet birch and oil of wintergreen are prepared, the yield of the latter oil is so small, that most of the so-called "oil of wintergreen" is really obtained from birch.

The differentiation between these two oils is a matter of considerable difficulty. In fact, no less an authority than Professor Kremers claims that it is practically impossible to decide chemically whether a given sample is from wintergreen or from birch. The present Pharmacopœia cites as a distinction that oil of birch is optically inactive, while oil of gaultheria is slightly levogyrate. Hurley claims that the three forms of methyl salicylate can be distinguished by their freezing points: oil of gaultheria, −86° C.; oil of betula, −42° C.; synthetic methyl salicylate, −30° C.

The difficulty in differentiating between oils of birch and wintergreen is due to the fact that both oils consist of from 99.0 to 99.8 per cent of methyl salicylate, hence the chemicals upon which differentiating tests are based are present in very small amounts. It is stated that the levogyrate constituent of oil of wintergreen is an ester, $C_{14}H_{42}O_2$.

As methyl salicylate can be made by combining methyl hydroxide and salicylic acid, so oil of wintergreen and oil of birch can be split up into these two constituents by the process of treating the oil with sodium hydroxide, when the methyl salicylate is decomposed by the following reaction:

$$CH_3C_7H_5O_3 + NaOH = CH_3OH + NaC_7H_5O_3.$$

This process of breaking down an ester is called *saponification*, because the formation of soap from a fixed oil—an ester of glycerin—is accomplished by a practically identical process. (See p. 742.)

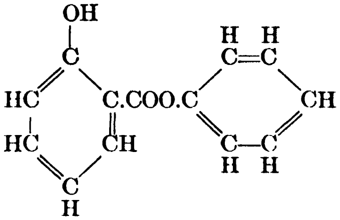
The saponification of the oil of wintergreen under the influence of sodium hydroxide is applied commercially in the manufacture of the so-called "natural salicylate of sodium" and "salicylic acid." The process is a simple one, the oil being warmed in a porcelain dish on a water bath, and then treated with molecular proportions of a solution of soda, when the sodium salicylate separates out in a white mass. On adding water the sodium salicylate dissolves, the solution is then filtered, and sodium salicylate obtained from the solution by granulation through evaporation. In preparing sodium salicylate by this process it is important that there be a slight excess of acid, otherwise the finished product will have an ugly gray color. Scrupulous pains must be taken to avoid any contact with iron during the manufacture, for the slightest trace of iron will color the sodium salicylate from pink to red. From this sodium salicylate a natural salicylic acid can be isolated by treatment with the requisite quantities of sulfuric acid and crystallization of the separated salicylic acid from alcohol.

These three forms of methyl salicylate are used as antirheumatics, but the less irritating sodium salicylate is usually preferable.

Dose.—0.75 cc. (12 minims).

PHENYLIS SALICYLAS—Phenyl Salicylate
(Phenyl. Salicyl.—Salol)

$C_{13}H_{10}O_3$



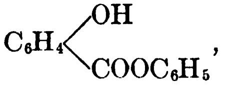
Molecular weight, 214.08

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

White crystalline powder; aromatic odor; characteristic taste; soluble in about 6670 parts of water and in about 5 parts of alcohol; also soluble in chloroform, ether, benzene, fixed and volatile oils; melts between 41° and 43° C. For details, see U.S.P., p. 288.

For *tests for identity* and for *impurities* (free acid, uncombined phenol or salicylic acid, sulfate, chloride), see U.S.P., p. 288.

Remarks.—The formula,  $C_6H_4\begin{cases}OH\\COOC_6H_5\end{cases}$, shows that salol is salicylic acid with the carboxyl hydrogen replaced by the phenyl group (C_6H_5). It can also be written as phenyl salicylate, $C_6H_5C_7H_5O_3$.

Salol is an artificial ester obtained by the treatment of phenol with salicylic acid in the presence of phosgene, sulfuric acid not being indicated in this case, since its action would be too violent. The equation of manufacture is—

$$C_6H_5OH + HC_7H_5O_3 = C_6H_5C_7H_5O_3 + H_2O.$$

Like phenol, salol liquefies when triturated with menthol, camphor, thymol, sulfonal or betanaphthol.

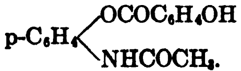
Salol has been found admirable in rheumatic cases, it having a less irritating action than have the other salicylates.

Salol is interesting because insoluble in acids, but freely soluble in alkalis. On account of this peculiarity it is used for a coating for enteric pills, such pills being designed to pass through the acid juices of the stomach undissolved, but intended to dissolve in the alkaline fluid of the intestines (p. 339).

Incompatibilities.—See prescriptions Nos. 73, 75, and 95 in Chapter LIX.

Dose.—300 mg. (5 grains).

So successful has salol proved that a large number of derivatives from it are now found on the market.

Salophen is acetyl-para-amido-salol, p-  $C_6H_4\begin{cases}OCOC_6H_4OH\\NHCOCH_3\end{cases}$**.**

The structure of this body can be best explained by the stages of its manufacture.

Salol is converted into para-nitro-salol, $p\text{-}C_6H_4\left\langle\begin{array}{l}OCO-C_6H_4OH\\NO_2\end{array}\right.$. This, by reduction, gives para-amido-salol, $p\text{-}C_6H_4\left\langle\begin{array}{l}OCO-C_6H_4OH\\NH_2\end{array}\right.$, and this, treated with acetic acid, yields salophen.

Salophen is used as a salol substitute in rheumatic and gastric troubles, it being considered safer than salol.

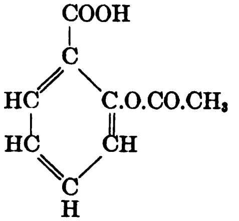
Saliphen, $C_6H_4\left\langle\begin{array}{l}OC_2H_5\\NHC_7H_5O_2\end{array}\right.$.—This body is a salicyl-phenetidin, and is mentioned in passing merely to call attention to the confusing similarity of the names of these two substances.

Salicylamide, $C_6H_4\left\langle\begin{array}{l}CONH_2\\OH\end{array}\right.$.—This is made by treating oil of wintergreen with ammonia gas, and is used as a salicylic acid substitute.

ACIDUM ACETYLSALICYLICUM—Acetylsalicylic Acid

(Acid. Acetylsal.—Aspirin)

$C_9H_8O_4$



Molecular weight, 180.06

Acetylsalicylic Acid, when dried to constant weight over sulfuric acid, contains not less than 99.5 per cent of $HC_7H_4O_2C_2H_3O_2$.

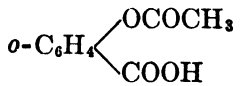
Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless crystals or needles or white powder; decomposes on contact with moisture; soluble in about 300 parts of water and about 4 parts of alcohol; also soluble in chloroform and ether; soluble with decomposition in solutions of alkaline hydroxides and carbonates; melts at not less than 135° C. For details, see U.S.P., p. 14.

For *tests for identity,* for *impurities* (carbonizable substances, coloring matter, resinous substances, free salicylic acid, chloride, sulfate, heavy metals) and for *assay,* see U.S.P., p. 15.

Remarks.—Acetylsalicylic acid, which was introduced under the trademarked name *aspirin,*



$$o\text{-}C_6H_4\left\langle\begin{array}{l}OCOCH_3\\COOH\end{array}\right.$$

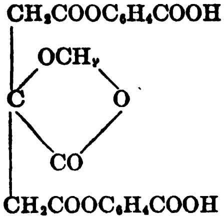
is salicylic acid in which the hydrogen of the hydroxyl group has been replaced by the acetyl group. It is made by heating salicylic acid with acetic anhydride. It occurs in colorless crystalline needles melting at 135° C. An aqueous solution slowly hydrolyzes on standing into the constituent acids. It is enormously popular as a substitute for salicylates.

Dose.—300 mg. (5 grains).

The extended use of acetylsalicylic acid renders it advisable to state that large doses have been known to produce toxic effects. Jordan reports that capsules containing Dover's powder, phenacetin and acetylsalicylic acid produced narcotic effects resembling those of heroin (p. 926).

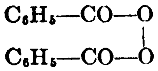
Ammonium acetylsalicylate and *Aluminum acetylsalicylate* have been recommended for use in fevers.

Novaspirin (N.N.R.) or *Salicitrin* is methylene-citryl-salicylic acid:



representing the citric acid molecule to which one oxy-methylene and two salicylic groups have been attached. Its use is similar to aspirin.

Benzoyl Peroxide,



$$\begin{array}{l} C_6H_5\text{—}CO\text{—}O \\ \qquad\qquad\quad\ \ | \\ C_6H_5\text{—}CO\text{—}O \end{array}$$

is a crystalline organic peroxide that is used rather largely as an antiseptic and a bleach for oils. Lamson finds it of value in ivy poisoning.

Quinic Acid is tetrahydroxyhexahydrobenzoic acid. (See p. 936.)

DIOXYBENZOIC ACIDS

We have already seen that salicylic acid is a mono-oxybenzoic acid, or a phenol in which 1 atom of hydrogen has been replaced by the carboxyl group. In the same way the dioxyphenols, by substitution of 1 atom of hydrogen with carboxyl, yield dioxybenzoic acids.

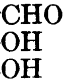
Thus, pyrocatechin, o-$C_6H_4(OH)_2$, yields protocatechuic acid, $\overset{(OH)_2(3:4).}{C_6H_3COOH(1).}$

Resorcin, m-$C_6H_4(OH)_2$, yields resorcylic acid, $\overset{(OH)_2(3:5).}{C_6H_3COOH(1).}$

Hydroquinine, p-$C_6H_4(OH)_2$, yields gentisinic acid, $\overset{(OH)_2(2:5).}{C_6H_3COOH(1).}$

These acids are of little importance in pharmacy.

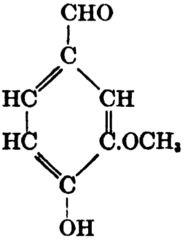
Gentisinic acid is a decomposition product of gentisin (p. 716), and protocatechuic acid is of interest only by reason of an important derivative of its aldehyde.

Protocatechuic aldehyde has the formula  $C_6H_3\begin{cases} CHO \\ OH \\ OH \end{cases}$, and the methyl ether of this aldehyde is vanillin.

VANILLINUM—Vanillin

(Vanillin.)

$C_8H_8O_3$



Molecular weight, 152.06

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Fine, white or faintly yellow, crystalline needles; soluble in about 100 parts of water and in alcohol, glycerin, chloroform or ether; optically inactive; melts between 80° and 82° C. For details, see U.S.P., p. 429.

For *tests for identity* and for *impurity* (acetanilid), see U.S.P., p. 429.

Remarks.—Vanillin is the odorous principle of the vanilla bean, which has long been popular as a flavoring agent. The extraction of vanillin from vanilla beans is a matter of comparatively little difficulty, but the small yields caused its commercial extraction to be at a cost almost prohibitive. The researches of Tiemann, however, proved the structural formula of the substance, and when this was known, the investigator found it a matter of no great difficulty to prepare vanillin from cheaper sources than from vanilla beans. The first vanillin made synthetically was made from coniferin found in the cambial juices of some species of pine. Vanillin from this source was prepared by Tiemann and Haarmann in their chemical factory at Holzminden, and soon became an article of commerce. A few years later, however, Tiemann discovered a simpler and more economic source of the production of vanillin in eugenol, a constituent of the oil of cloves, from which it is obtained by oxidation with potassium permanganate, or with ozone.

Vanillin occurs in the form of white crystals, melting at 81° C., freely soluble in alcohol, and much less so in water. It possesses a delightful odor of the vanilla beans, and is now very largely used instead of vanilla beans, both in flavoring extracts and particularly in perfumery.

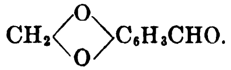
Protocatechuic Ethyl Ether, $C_6H_3.CHO.OH.OC_2H_5$, is now an article of commerce under such trade names as *bourbonal* and *vanirom*. It is claimed to possess four times the flavoring value of vanillin.

Capsaicin, the pungent principle of capsicum (see p. 859), is vanillin-decenoyl amide. Nelson has prepared 14 synthetic amides of vanillin and found most of them pungent.

Vanilla (N.F. VI), is the cured, full grown, unripe fruit of *Vanilla planifolia* Andrews (Fam. *Orchidaceæ*). It contains vanillin, volatile oil, fixed oil, resin, sugar and mucilage. There is a great variation in quality of commerce vanilla beans, ranging from Mexican beans, the finest, to the Tahiti bean, the poorest—so poor that they should not be used. The poorer the quality, the more mucilage and less aroma the bean possesses. Vanilla is used almost entirely as a flavor.

Tonka Bean is the seed of *Coumarouna odorata* and contains coumarin. It is used as an aromatic in adulterating extract of vanilla.

Piperonal or *Heliotropin* is the methylene ether of protocatechuic aldehyde:



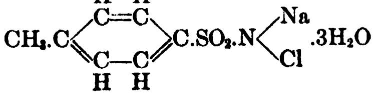
$$CH_2\left\langle\begin{matrix}O\\O\end{matrix}\right\rangle C_6H_3CHO.$$

It occurs in white scales melting at 37° C. and has the pleasant odor of heliotrope. For this reason, it has large use in perfumery (p. 836).

Chloramines.—While Dakin's Solution (see p. 211) is an admirable wound antiseptic, its instability led to a search for more stable chlorine antiseptics. This search brought to light two satisfactory organic chlorinated bodies, *chloramine-T* or paratoluene sodium sulfonchloramide, $CH_3C_6H_4SO_2NaNCl$, and *dichloramine-T* or paratoluene sulfondichloramide, $CH_3C_6H_4SO_2NCl_2$. These are made as by-products in the manufacture of saccharin or can be produced directly from toluene. Both are recognized in U.S.P. XI.

CHLORAMINA-T—Chloramine-T

(**Chloram.-T**—Chloramina U.S.P. X, Chloramine)



$C_7H_7O_2NSClNa.3H_2O$ **Molecular weight, 281.62**

Sodium Paratoluenesulfonchloramide contains the equivalent of not less than 11.5 per cent and not more than 13 per cent of active Cl.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White or faint yellow crystals or powder; odor of chlorine; loses chlorine on exposure to air; soluble in about 7 parts of water; decomposed by alcohol; insoluble in benzene, chloroform and ether. For details, see U.S.P., p. 117.

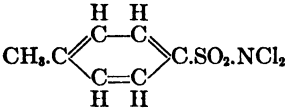
For *tests for identity*, for *impurities* (dichloramine, carbonizable substances) and for *assay*, see U.S.P., p. 118.

Remarks.—This official has been described above. It is used as a wound dressing in a 1 to 2 per cent aqueous solution and is applied in the way in which Dakin's solution is employed.

DICHLORAMINA-T—Dichloramine-T

(Dichloram.-T—Dichloramina U.S.P. X, Dichloramine)

$C_7H_7O_2NSCl_2$



Molecular weight, 240.04

Paratoluenesulfondichloramide, containing the equivalent of not less than 28 per cent and not more than 30 per cent of active Cl.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Pale yellow crystals or yellow powder; odor of chlorine; loses chlorine on exposure to air; almost insoluble in water; soluble in eucalyptol, in chlorinated paraffin and in glacial acetic acid; also soluble in benzene, chloroform and carbon tetrachloride; decomposed by alcohol. For details, see U.S.P., p. 135.

For *tests for identity*, for *impurity*, (chloramine) and for *assay*, see U.S.P., p. 135.

Remarks.—This official has been discussed above. It contains over twice as much active chlorine as chloramine and is an effective germicide. Being almost insoluble in water, it is applied as a wound dressing as a 5 per cent solution in *chlorocosane* (p. 644).

BIBLIOGRAPHY

Toluene.—(Manufacture) Pelletiere and Walter, Ann. chim. phys., [2], 67, 1838, 278; Deville, Ann. chim. phys., [3], 3, 1841, 168; Friedel and Craft, Ann. chim. phys., [6], 1, 1884, 459; Fittig, A., 131, 1864, 303; Anon., Jl. Am. Chem. Soc., 33, 1911, 47; Egloff, Jl. Ind. Eng. Ch., 10, 1918, 8; Wheeler, *ibid.*, 10, 1918, 359.

Friedel-Craft Reaction.—Schlaarschmidt, C.A., 18, 1924, 2875; Ashdown, Jl. Ind. Eng. Ch., 19, 1927, 1063; Groggins, C.A., 25, 1931, 687.

Cresols.—Schultze, B., 20, 1887, 410; Delplanque, A.J.P., 60, 1888, 510; Hammer, Jl. ph. ch., 25, 1892, 118; Lacroix, *ibid.*, 28, 1893, 349; Weger, Z. angew. Ch., 22, 1909, 393; Couch, Yearbook, A.Ph.A., 7, 1918, 450; Gibbs, Jl. Am. Ch. Soc., 49, 1927, 839.

Compound Solution of Cresol.—Gerlach, A.Ph.A., 39, 1891, 356; Anon., Pract. Dr., 28, 1910, 57.

Chloramines.—Dakin and co-workers, C.A., 10, 1916, 1363; Sweet, C.A., 11, 1917, 3337; Cook, Proc. N. J. Ph.A., 48, 1918, 41; Inglis, Jl. Soc. Ch. Ind., 37, 1918, 288T; Krauss, A.J.P., 90, 1918, 16; Dunham, Jl. A.M.A., 70, 1918, 571; Griffith, Am. Dr., 66, 1918, 5; Hessler, A.J.P., 90, 1918, 424; Carnot and Bondony, *ibid.*, 91, 1919, 474; Lee, *ibid.*, 91, 1919, 123; Deplas, *ibid.*, 91, 1919, 697; Harris, Jl. A.Ph.A., 9, 1920, 39; Krais and Meves, Jl. Soc. Ch. Ind., 44, 1925, 735B; Schlemmer, Ph. Zent., 68, 1927, 791; King and Smith, C.A., 26, 1932, 4395.

Creosol.—Hlasiwetz, A., 106, 1858, 384.

Creosote.—(Etymology) Rice, A.J.P., 66, 1894, 166. (History) Schorlemmer, Ph. Jl., [3], 15, 1885, 1046. (Manufacture) Reichenbach, Jl. de Ph., 19, 1833, 544. (Constituents) Hlasiwetz, A., 106, 1858, 384; Gorup-Besanez, A., 143, 1867, 129; Sickman and Fischelis, Jl. A.Ph.A., 18, 1929, 1145. (Tests) Flückiger, Ph. Jl., [3], 2, 1872, 1008; Morson, *ibid.*, [3], 2, 1872, 921. (Coal-tar creosote) Mittelbach, A.Ph.A., 50, 1902, 374; Merck, A.Ph.A., 49, 1901, 275.

Benzyl Alcohol.—(Manufacture) Anon., A.J.P., 91, 1919, 297; Hobart, Ph. Jl., 113, 1924, 635. (Properties) Anon., C.A., 13, 1919, 2107. (Medical uses) Macht, Jl. A.M.A., 70, 1918, 1893; C.A., 13, 1919, 2710; Jl. A.Ph.A., 11, 1922, 897; Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 456.

Benzaldehyde.—(Manufacture) Canizzaro, Ann. chem. phys., [3], 40, 234.

Oil of Bitter Almond.—(Manufacture) Kremers and Schreiner, Ph. Rev., 14, 1896, 197; Eck, A.Ph.A., 32, 1884, 262; Feist, Arch. d. Pharm., 246, 1908, 206.

Bitter Almond.—(Constituents) Robiquet and Vogel, Jl. de Ph., 8, 1822, 293; Boutron-Charlard, Jl. de Ph., 17, 1831, 144; Portes, A.J.P., 50, 1870, 71; Osborne and Campbell, Jl. Am. Ch. Soc., 18, 1896, 610; Rosenthaler, Ber. d. Pharm. Ges., 32, 1922, 237. (Properties) Pitman, Jl. Ind. Eng. Ch., 22, 1930, 1129. (Amygdalin) Karrer, Nägeli and Lang, C.A., 15, 1921, 61; Haworth and Leitch, *ibid.*, 16, 1922, 4191; Hudson, Jl. Am. Ch. Soc., 46, 1924, 483; Rosenthaler, Arch. d. Pharm., 263, 1925, 563; Ed., Jl. Soc. Ch. Ind., 49, 1930, 1001.

Wild Cherry.—(Source) Moser, A.Ph.A., 58, 1910, 208. (Constituents) Power and Moore, C.A., 3, 1909, 1529; Peacock, A.J.P., 95, 1923, 613. (Pharmacy) Moore, A.J.P., 45, 1873, 244.

Benzoic Acid.—(Manufacture) Procter, A.J.P., 27, 1883, 23; Ott, Ch. News, 17, 1868, 69. Rad., Ding. Pol. Jl., 231, 1879, 451; Lunge, B., 10, 1877, 1275. (Preservative action) Remsen, F. I. D., 104 (1909); Serger, Ch. Zt., 35, 1911, 1127, 1150, 1160, 1194, and 1202. (Tests) A. B., C.A., 23, 1929, 5544. (Deterioration) Arny and coworkers, Jl. A.Ph.A., 20, 1931, 1153.

Ortho-aminobenzoic Acid.—Sale and Wilson, Jl. Frank. Inst., 202, 1926, 663.

Benzyl Benzoate.—Macht, Yearbook, A.Ph.A., 8, 1919, 448 and 9, 1920, 590; Jl. A.Ph.A., 11, 1922, 897; Volweiler and Vliet, Jl. A.C.S., 43, 1921, 1672; Shonle and Rowe, *ibid.*, 43, 1921, 361; Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 456.

Anesthesin.—Hirschfelder, see above; Smith, Drug and Cosmet. Ind., 35, 1934, 142.

Butesin Picrate.—Thayer, A.J.P., 97, 1925, 39.

Nipagin.—Augustin, Pract. Dr., 50, Nov., 1932, 30; Sabalitschka, Ph. Acta Helv., 5, 1930, 286.

Benzosulphinide.—(Manufacture) Remsen and Fahlberg, Am. Ch. Jl., 1, 1879, 426. (Properties) Dohme, Am. Dr., 19, 1890, 122. (Sweetness) Paul, Jl. Soc. Ch. Ind., 40, 1921, 33R; Helch, *ibid.*, 11, 1917, 2532. (Therapeutics) Remsen, F. I. D., 135 (1911). (Pharmacy) Miller, Dental Cosmos, 33, 1891, 917. (Substitutes) Taufel and Wagner, C.A., 19, 1925, 2347; Uhthoff and Moragas, C.A., 23, 1929, 1889; Oddo and Mingoia, C.A., 21, 1927 and 26, 1932, 122.

Saligenin.—Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 457.

Salicylic Acid.—(History) Sharp, Ph. Jl., 94, 1915, 857; Piria, A., 30, 1839, 151; Merrell, Pract. Dr., 29, 1911, 23. (Source) Cahours, Jl. de Ph. et Ch., [3], 3, 1843, 364. (Syntheses) Hesse, A.Ph.A., 37, 1889, 265. (Manufacture) Anon., Ch. and Dr., 85, 1914, 313. (Preservative action) Serger, Ch. Zt., 35, 1911, 1194. (Tests) Anon., A.J.P., 54, 1882, 443. (Incompatibilities) Hill, Ph. Jl., 116, 1926, 358. (Iron salicylates) Claasz, Arch. Pharm., 253, 1915, 342 and 360; Knott, Ph. Jl., 124, 1930, 194. (Pharmacology) Holmes, C.A., 20, 1926, 231.

Acetylsalicylic Acid.—Anon., Ch. and Dr., 85, 1914, 314; Parry, Ch. and Dr., 88, 1916, 611; Anon., Jl. A.M.A., 72, 1919, 119; Ruddiman, Jl. A.Ph.A., 11, 1922, 796; Snidow and Langenhan, *ibid.*, 14, 1925, 125 and 694. (History) Armstrong, 50, 1931, 262. (Manufacture) Anon., Ch. Zt., 51, 1927, 411. (Properties) Putnam, Jl. Ind Eng. Ch., 16, 1924, 778; Germuth, Jl. A.Ph.A., 20, 1931, 568. (Tests) Paul, C.A., 18, 1924, 3251; Valentin, C.A., 26, 1932, 3328. (Toxicity) Jordan and Klemme, Jl. A.Ph.A., 18, 1929, 810; Krasso, C.A., 24, 1930, 1425.

Ammonium Acetylsalicylate.—Woldman, Jl. A.Ph.A., 18, 1929, 14.

Aluminum Acetylsalicylate.—Anon., Jl. Ind. Eng. Ch., News Supp., 11, 1933, 54.

Methyl Salicylate.—(History) Cahours, Jl. de Ph. et Ch., [3], 3, 1843, 364; Procter, A.J.A., 14, 1842, 211 and 15, 1843, 243.

Oil of Gaultheria.—(History) Anon., A.J.P., 6, 1834, 289; Procter (above). (Tests) Gesell, Pract. Dr., 32, 1915, 25; Hurley, Pract. Dr., 39, Nov., 1921, 21; Anon., Pract. Dr., 50, May, 1932, 26.

Oil of Birch.—(History) Procter, see above. (Tests) Kremers, A.Ph.A , 50, 1902, 378; Hurley, see above; Anon., C.A., 18, 1924, 3682

Salol.—(History) Nencki, Am. Dr., 15, 1886, 226. (Structure) Anon., Ph. Cent., 28, 1887, 158. (Manufacture) Kolbe, Ph. Zt., 31, 1886, 544. (Properties) Watring, A.J.P., 82, 1910, 241. (Incompatibilities) Bianchini, C.A., 8, 1914, 3488. (Enteric coating) Gerhard, A.Ph.A., 42, 1894, 592.

Benzoyl Peroxide.—Vanino and Herzer, Arch. Pharm., 253, 1915, 426; Farmer, Jl. Soc. Ch. Ind., 40, 1921, 84T; Lamson, A.J.P., 102, 1930, 596.

Quinic Acid.—Emde, C.A., 12, 1920, 2543.

Vanillin.—(Structure) Erlenmeyer, B., 9, 1876, 273. (Synthesis) Tiemann, B., 7, 1874, 605 and 8, 1875, 509, 1123 and 1127. (Manufacture) Busse, A.J.P., 72, 1900, 379; Tiemann and Haarmann, B., 8, 1875, 1115; Wood, C.A., 17, 1923, 2418; Fichter, Jl. Soc. Ch. Ind., 48, 1929, 329T; Schwyzer, *ibid.*, 50, 1931, 57B. (Properties) Mange and Ehler, Jl. Ind. Eng. Ch., 16, 1924, 1258. (Substitutes) Defren, C.A., 24, 1930, 440; Dingemans, C.A., 25, 1931, 1296.

Capsaicin.—Nelson, Jl. A.C.S., 41, 1919, 2121 and 45, 1923, 2179.

Vanilla.—(History) Jackson, A.J.P., 47, 1875, 317; Hires, A.J.P., 65, 1893, 571. (Cultivation and curing) Rabak, Jl. Ind. Eng. Ch., 8, 1916, 815; Mawby, Pract. Dr., 39, Nov., 1920, 60; Anon., *ibid.*, 39, Jan., 1920, 37; Barnes, Dr. Circ., 65, 1921, 262; Cunningham, A.J.P., 93, 1921, 272; Anon., Ph. Jl., 128, 1932, 268. (Constituents) Gobley, Jl. de Ph. et Ch., 34, 1858, 401; Leutner, Ch. News, 25, 1872, 83; Dean and Schlotterbeck, Jl. Ind. Eng. Ch., 8, 1916, 607 and 703; Goris, C.A., 18, 1924, 3205. (Varieties) Busse, A.Ph.A., 58, 1910, 167; Gautier and Kling, C.A., 4, 1920, 2337. (Extraction) Dean and Schlotterbeck, see above; Wilson and Sale, Jl. Ind. Eng. Ch., 15, 1923, 782.

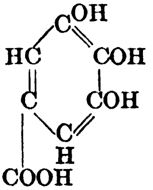
Tonka Bean.—Albes, Mid. Dr., 50, 1916, 109.

CHAPTER XLV

GALLIC AND TANNIC ACIDS. ASTRINGENT DRUGS

IN the preceding chapter we have described benzoic acid, C_6H_5COOH, hydroxybenzoic acid or salicylic acid, $C_6H_4\substack{OH\\COOH}$, and 3 dihydroxybenzoic acids, $C_6H_3\substack{(OH)_2\\COOH}$. We now turn to the trihydroxybenzoic acids, $C_6H_2\substack{(OH)_3\\COOH}$ and one of these, *gallic acid*, is not merely an important medicament itself, but may also be considered the foundation stone of those valuable plant bodies, the *tannins*.

Acidum Gallicum (U.S.P. IX; N.F. VI), or *Gallic Acid*, has the formula, $C_6H_2(OH)_3$-COOH or $HC_7H_5O_5$; graphically

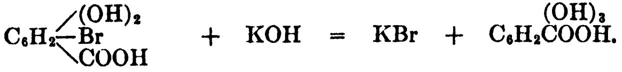


In short, it is benzene with 3 hydrogen atoms replaced by hydroxyl groups and one hydrogen replaced by a carboxyl group.

Gallic acid was isolated from nutgall by Scheele in 1785, who gave it the name from the source of its supply.

Gallic acid can be made synthetically by fusing of bromoprotocatechuic acid with potassa, as shown in the following equation:

Bromoprotocatechuic acid — Gallic acid



$$C_6H_2\begin{cases}(OH)_2\\ Br\\ COOH\end{cases} + KOH = KBr + C_6H_2\overset{(OH)_3}{}COOH.$$

It is usually obtained by macerating nutgalls with water long enough (several weeks) to hydrolyze the tannin into gallic acid. The cold acid aqueous liquid, in which but little gallic acid and much of the foreign matter dissolves, is expressed and thrown away. The press cake is then treated with boiling water, in which the gallic acid freely dissolves, and the hot infusion set aside to permit crystallization of the acid.

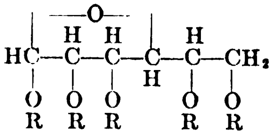
Gallic acid is a valuable astringent, of particular service as a harmless agent for stopping minor hemorrhages, such as nosebleed. In such case, snuffing a small quantity of gallic acid up the nose usually staunches the flow of blood. It is given as an intestinal astringent, and is also used externally; for this purpose the formerly official ointment of gallic acid is recommended.

Incompatibilities.—See prescription No. 83 in Chapter LIX.

Dose.—1 Gm. (15 grains).

While gallic acid is no longer official, one of its salts is accorded pharmacopœial recognition. This is *bismuth subgallate* (p. 602).

Tannins or *tannoids* are astringent plant principles, of which the official tannic acid is the most notable representative. For many years tannic acid was considered as digallic acid, $C_{14}H_{10}O_9$, or graphically, $C_6H_2(OH)_3COOC_6H_3(OH)_2COOH$; that is, 2 molecules of gallic acid, $C_7H_6O_5$, minus 1 molecule of water. Fischer, Freudenberg, Nierenstein and others, however, have shown that it is a mixture of digallic acid, $C_{14}H_{10}O_9$, with glucose and other bodies. Digallic acid minus a hydroxyl group becomes the *galloyl* radical and according to Fischer, nutgall (or Chinese) tannin is penta-galloyl-glucose;



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| & & | & & | & & H & & | & & | \\
O & & O & & O & & & & O & & O \\
R & & R & & R & & & & R & & R
\end{array}$$

the five "R's" being the galloyl group mentioned above.

Fischer succeeded in synthesizing this penta-galloyl-glucose, but while this closely resembles nutgall tannin, it is not identical with it, so the constitution of this tannin is not yet settled. Fischer prepared a number of synthetic tannins, one yielding an iodine derivative containing 426 atoms and having the molecular weight 4021. A confusing element in the tannin problem is the fact that while Chinese and Turkish tannins are both obtained from nutgalls they are not chemically identical. Thus, while Chinese tannin is a penta-galloyl compound, Turkish tannin appears to contain a lesser number of galloyl groups.

Nierenstein (1926) does not agree with the Fischer view, that tannin is a glucose compound. He believes it to contain no glucose and considers it as essentially a poly-digalloyl-leucodigallic acid anhydride.

It has long been known that the other plant tannins were not identical with the official nutgall tannin, although like it other tannins are glucosidal derivatives of gallic and similar acids. One of the earlier means of distinguishing the different tannins was based upon their behavior with iron salts, the production of either a green-black precipitate or a blue-black precipitate. Another classification of the tannins is that of Kunz-Krause, given below:

NONGLUCOSIDAL TANNOIDS: Such as gallic acid; protocatechuic acid, digallic acid, etc.

GLUCOSIDAL TANNOIDS:

(*a*) *Glycotannoids.*

Protocatechuic acid derivatives, such as cincho-tannic acid, caffe-tannic acid, etc.

Gallic acid derivatives, such as pomegranate root tannin, nutgall tannin.

(*b*) *Phloroglucin tannoids.*

Protocatechuic acid derivatives, such as quebracho-tannic acid, catechu-tannic acid, kola-tannin, etc.

Gallic acid derivatives, none yet known.

The protocatechuic acid derivatives mentioned above include those tannoids turning green-black with ferric chloride; while the "gallic acid derivatives" turn blue-black with ferric chloride.

ACIDUM TANNICUM—Tannic Acid

(Acid. Tan.—Gallotannic Acid, Tannin)

A tannin usually obtained from nutgall.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Yellowish-white or light brown amorphous powder or glistening scales or spongy masses; very faint characteristic odor; strongly astringent taste; soluble in about 1.25 parts of glycerin when gently warmed; quite soluble in water, alcohol and diluted alcohol; less so in dehydrated alcohol; almost insoluble in ether, chloroform, benzene and petroleum benzin. For details, see U.S.P., p. 29.

For *tests for identity* and for *impurities* (gum, dextrin, resinous substances), see U.S.P., p. 30.

Remarks.—The tannin of the Pharmacopœia is obtained from nutgall and is frequently called gallotannic acid. It will be noticed in the pharmacopœial description that an aqueous solution of tannin precipitates gelatin from its solution (see clarification, p. 161) as a substance akin to leather. Fresh animal hide consists of collagen combined with a mass of animal fibers, and when this is macerated in a solution of tannin (generally from oak bark), it is converted into leather supposedly by adsorption. (See p. 156.)

The deep blue-black precipitate produced by the treatment of tannin with ferric chloride solution is the basis of most of our writing ink, which is made by treating nutgall infusion with iron salts and adding some gummy substance which will hold the colloidal form of the resulting chemical suspension.

Tannin is obtained by exposing powdered nutgalls to a damp atmosphere for several days, and then macerating with a small quantity of ether, and expressing the liquid, repeating the maceration and expression with ether containing one sixteenth its bulk of water. The reason of this process of extraction is puzzling, since the tannin so obtained is practically insoluble in strong ether. Tannin can also be extracted from nutgall with a mixture of alcohol and ether, and in a patented process acetic ether is the solvent employed.

Tannic acid is one of the most valuable astringents, and is used both internally and externally. When used internally, it is given for diarrhea. For this purpose, however, it is usually advisable to administer a tannin-bearing drug, such as catechu or krameria. Latterly a number of "masked tannin" compounds, such as tannin proteins, tannin acetyl esters, tannin formaldehyde preparations, have been introduced.

Externally, it is used to staunch the flow of blood, and for gargles in sore throat and as an application for piles. In the form of a 2.5 per cent sterile aqueous solution, tannic acid is now largely used by spraying as an application for burns.

Dose.—As antidote, 1·Gm. (15 grains).

Incompatibilities.—See prescriptions Nos. 34 and 83 in Chapter LIX.

The official preparations of tannin are *glycerite of tannic acid* and *ointment of tannic acid.*

ACIDUM ACETYLTANNICUM—Acetyltannic Acid

(Acid. Acetyltan.—Diacetyltannic Acid, Tannyl Acetate, Acetannin)

Acetyltannic Acid is a product obtained by the acetylation of tannic acid.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Yellowish-white on grayish-white powder, darkening on exposure to light; odorless or of a slight acetous odor; sparingly soluble in water and alcohol; soluble in ethyl acetate; soluble with decomposition in solutions of alkaline hydroxides or carbonates. For details, see U.S.P., p. 16.

For *tests for identity* and for *impurities* (free acid, free tannic acid, soluble substances), see U.S.P., p. 16.

Remarks.—This official was originally introduced under the trade-marked name, *tannigen.* It is a yellowish or grayish-white powder only sparingly soluble in water but soluble with decomposition in alkaline solutions. It is therefore recommended in diarrhea, since it scarcely dissolves in the acid juices of the stomach but does dissolve in the alkaline fluid of the intestines.

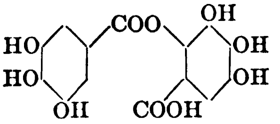
Dose.—600 mg. (10 grains).

Depsides.—The word "depside" was coined by Fischer to designate products of the condensation of two or more molecules of the hydroxy-acids of benzene. The simplest depside is digallic acid, $C_{14}H_{10}O_9$, described above, and Fischer synthesized a large number of others.

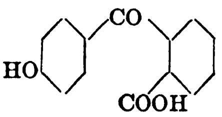
Chlorogenic Acid is a depside of caffeic and quinic acids. It has the formula, $C_6H_3(OH)_2CH{=}CHCOOC_6H_7(OH)_3COOH$, is a product of the hydrolysis of caffetannic acid and is found in a number of plants of the *Araliacæ.*

Phlobaphenes are water-insoluble red-brown tannin derivatives. Structurally they stand between the depsides and the oxyanthraquinones (see p. 892) as represented schematically below:

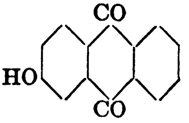
Digallic acid



Phlobaphene (presumably)

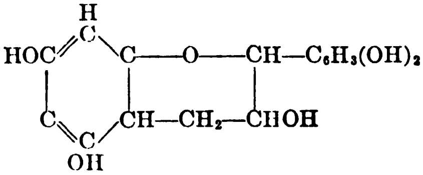


Oxyanthraquinone



Phlobaphenes are found in a number of drugs, such as cinchona, cinnamon, rhatany and clove. The turning brown of a sliced apple and the change in color of the kola nut and the cacao bean during their curing are due to the transformation of tannoid substances into phlobaphenes.

Catechin is a crystalline principle obtained from gambir and catechu. It is the mother substance of the tannins from these drugs. Freudenberg believes its formula is



DRUGS CONTAINING ASTRINGENT PRINCIPLES

Krameria (U.S.P. X; N.F. VI), or *Rhatany,* is the dried root of *Krameria triandra* and *K. argentea.* The former species is known as Peruvian rhatany while the latter species is the Para or Brazilian variety. Krameria contains kramerotannic acid, which consists of pure tannin, phlobaphene and extract; krameric acid; rhatanin, $HO—C_6H_4-CH_2CH(NHCH_3)COOH$; red coloring matter; starch. It is used as an astringent. The fluidextract (p. 271) is official in the Formulary.

Dose.—1 Gm. (15 grains).

Geranium (U.S.P. VIII; N.F. V), or *Cranesbill,* is the dried rhizome of *Geranium maculatum* Linné (Fam. *Geraniaceæ*). It contains tannin, gallic acid, mucilage and resin, and is used as an astringent in 15 grain doses.

Rubus (U.S.P. VIII; N.F. V), or *Blackberry Root* is the dried bark of the rhizome of *Rubus villosus* Aiton, *Rubus nigrobaccus* Bailey, or of *Rubus cuneifolius* Pursh (Fam. *Rosaceæ*). It contains tannin, *villosin* (bitter glucoside), etc., and is used as an astringent in 15-grain doses.

Hæmatoxylon (U.S.P. VIII; N.F. V), or *Logwood,* is the heart wood of *Hæmatoxylon campechianum* Linné (Fam. *Leguminosæ*), that has not undergone fermentation. It contains tannin and *hematoxylin,* a neutral principle having the formula $C_{16}H_{14}O_6$, (p. 882) and giving the wood its color.

The "heart wood" means the heavier older wood found in the interior of a trunk. Its technical name is the "duramen," while the lighter, younger, outer wood is called the "alburnum." The hematoxylin, mentioned above, has chemical value as an indicator in volumetric analysis (p. 1005).

Chief use of logwood is in dyeing, a decoction of the wood mixed with copperas coloring fabrics a deep black. For dyeing purposes, however, the wood is generally submitted to a fermentation process, when it assumes a green, metallic luster. Such wood should not be used in medicine. Hematoxylon is used as an astringent usually in the form of the extract.

Hamamelidis Cortex (U.S.P. VIII; N.F. V), or *Witch Hazel Bark*, is the bark and twigs of *Hamamelis virginiana* Linné (Fam. *Hamamelidaceæ*). It contains tannin (a digalloyl hexose), bitter principle, chlorophyll and trace of volatile oil. It is an astringent of little value, used in making *hamamelis water* (p. 201).

Dose.—30 grains.

Hamamelidis Folia (U.S.P. VIII; N.F. V), or *Witch Hazel Leaves*, are the dried leaves of *Hamamelis virginiana* Linné (Fam. *Hamamelidaceæ*), collected in autumn, before the flowering of the plants. The drug contains tannin and a trace of volatile oil and is used as an astringent, in 30-grain doses.

Quercus (U.S.P. VIII; N.F. V), or *White Oak Bark*, is the dried bark of the trunks and branches of *Quercus alba* Linné (Fam. *Fagaceæ*) deprived of the periderm, or the outer corky layer of the bark. It contains tannin (quercitannic acid), oak red and pectin and is used as an astringent in 15-grain doses.

Rosa (U.S.P. X; N.F. VI) is the dried petals of *Rosa gallica*. It contains a tannin (*rosatannic acid*), no gallic acid, trace of volatile oil, quercetin, color, etc. The coloring matter consists of a red *anthocyanin* (p. 882) which hydrolyzes to phloroglucinol (p. 779), a pyrone nucleus and protocatechuic acid and a yellow dye identical with quercetin (pp. 882 and 883).

Rose is used as an astringent tonic. *Rose honey* (U.S.P. X) was formerly highly esteemed as a wash for sore mouth. The Formulary preparations of rose are the *fluidextract* (p. 271) and *honey of rose and borax* (p. 225).

Rosa Centifolia (U.S.P. 1890), or *Pale Rose*, contains a trace of tannin, and was used chiefly as a flavor. Bear in mind that while the official *stronger rose water* (p. 200) is made from this rose, *oil of rose* comes from a different species. (See p. 842.)

GALLA—Nutgall

(Gall.)

Nutgall is the excrescence obtained from the young twigs of *Quercus infectoria* Olivier and other allied species of *Quercus* (Fam. *Fagaceæ*).

Constituents.—Tannin, 50 per cent (a glucosidal form that hydrolyzes to glucose and digallic acid); gallic acid, 3 per cent; pectose; a ferment (pectase), etc.

Remarks.—As already mentioned (p. 720) nutgall is the source of both official tannin and of gallic acid.

Medical Properties.—Valuable astringent. The official *ointment* (p. 419) is largely used for hemorrhoids.

Dose.—500 mg. (8 grains).

Gambir (U.S.P. X; N.F. VI), or *Pale Catechu*, is the dried aqueous extract prepared from the leaves and twigs of *Ourouparia Gambir*. It contains catechu-tannic acid; catechin (p. 811), quercetin (p. 882), etc. This drug replaces the formerly official catechu. It occurs in pale brownish-gray or light brown cubes, quite different in appearance from the dark brown catechu. It is used extensively as a dyestuff, coloring black when combined with iron salts. It is used as an astringent. Administered in diarrhea mixtures as the *compound tincture* (p. 253).

Dose.—0.5 Gm. (8 grains).

Catechu, the extract of the wood of *Acacia catechu*, was official until the eighth revision, when it was replaced by gambir, with which it is identical as far as constituents and medical properties are concerned.

KINO—Kino

Kino is the dried juice obtained from the trunk of *Pterocarpus Marsupium* Roxburgh (Fam. *Leguminosæ*).

Kino yields not less than 60 per cent of alcohol-soluble extractive and not less than 75 per cent of water-soluble extractive.

Constituents.—Kinotannic acid; kinoic acid, kinoin, $C_{14}H_{12}O_6$; kino red, $C_{20}H_{22}O_{11}$, etc.

Remarks.—The only point worth noting regarding kino is the fact, already mentioned (p. 249), that kino contains an enzyme which causes the tincture to gelatinize, unless the official recipe is strictly followed.

Medical Properties.—Astringent. Administered in diarrhea mixtures as *tincture* (p. 249).

Dose.—500 mg. (8 grains).

BIBLIOGRAPHY

Gallic Acid.—(History) Feist, Arch. d. Pharm., 251, 1913, 468. (Structure and synthesis) Barth and Sennhofer, A., 164, 1872, 119. (Extraction) Mueller, A.J.P., 18, 1847, 237; Weber, N.R., 9, 1880, 4.

Tannic Acid.—(History) Pelouze, Pogg. Ann., 29, 1834, 180. (Structure) Schiff, B., 4, 1871, 231, 967; Fischer and Freudenberg, B., 45, 1912, 1915; Nierenstein and co-workers, Ch. Zt., 34, 1910, 625; A., 338, 1912, 223 and C.A., 15, 1921, 1694; Jl. Am. Ch. Soc., 47, 1925, 850 and 1726 and Jl. Soc. Ch. Ind., 45, 1926, 221; Feist and Haun, Arch. d. Pharm., 251, 1913, 458; Fischer, B., 45, 1912, 915; 46, 1913, 3253; 52, 1919, 809 and 828; Ph. Zt., 65, 1920, 163; Freudenberg, Jl. Soc. Ch. Ind., 40, 1921, 312A; Hepworth, Jl. Soc. Ch. Ind., 42, 1923, 41T; Thomas, Jl. Ind. Eng. Ch., 14, 1923, 829. (Extraction) Bollay, A.J.P., 33, 1861, 337; Feist, Ch. Zt., 32, 1908, 918; Knape, C.A., 16, 1922, 1833. (Tests) Fear, Jl. Soc. Ch. Ind., 48, 1929, 296; Hoch, Jl. A.Ph.A., 22, 1933, 121. (Medical uses) Hanzlik, Jl. A.M.A., 72, 1919, 577; Sollmann, C.A., 15, 1921, 1544; Wilson, Jl. Soc. Ch. Ind., 48, 1929, 1074; Herzfeld, Ph. Jl., 122, 1929, 203; Hommell, Pract. Dr., 51, Feb., 1933, 12. (Tanning) Bennett, C.A., 12, 1918, 540; Wilson, *ibid.*, 11, 1917, 1564 and 14, 1920, 2275; DeJong, *ibid.*, 17, 1923, 2527.

Tannins.—(Sources) Czapek, C.A., 15, 1921, 3300. (Classification) Kunz-Krause, Ch. Zt., 20, 1896, 794. (Composition) Fischer, Freudenberg, Nierenstein, Hepworth, Thomas, see above.

Depsides.—Fischer, see above

Chlorogenic Acid.—Freudenberg, Jl. Soc. Ch. Ind., 39, 1920, 274A; Gorter, Ph. Week., 57, 1920, 194.

Phlobaphenes.—Nierenstein, B., 40, 1909, 4575; Dittmar, Jl. A.Ph.A., 12, 1923, 680; Bergmann and Pojarlieff, C.A., 25, 1931, 5155.

Catechin.—Kostanecki, B., 39, 1906, 4007; Freudenberg, B., 53, 1920, 1423 and 56B, 1923, 2127; Euler, C.A., 15, 1921, 2854; Nierenstein, B., 56B, 1923, 1877; Jl. Am. Ch. Soc., 46, 1924, 2793 and 2798; *ibid.*, 48, 1926, 1959; *ibid.*, 52, 1930, 1672; Mason, Jl. Soc. Ch. Ind., 47, 1928, 269T.

Krameria.—(Constituents) Soubeiran, Jl. de Ph., 19, 1833, 596; Goldschmied, Sch. Wsch. f. Ch. u. Ph., 51, 1913, 786.

Geranium.—(Constituents) Staples, A.J.P., 1, 1829, 171; Trimble and Peacock, A.J.P., 63, 1891, 265; Peacock, *ibid.*, 100, 1928, 548.

Rubus.—(Constituents) Krauss, A.J.P., 61, 1889, 605.

Hematoxylon.—(Source) Davis and Thomas, O.P.D. Rep., 93, 1918, No. 9, 22. (Constituents) Kramer, A.J.P., 54, 1882, 388; Erdmann, A., 216, 1882, 286. (Commercial) Bruehl, Am. Dr., 18, 1889, 195.

Hamamelis.—(Constituents) Freudenberg, C.A., 13, 1919, 1847; 14, 1920, 2639 and 3413; 19, 1925, 260; Scoville, A.J.P., 79, 1907, 496; Jowett and Pyman, Ph. Jl., 91, 1913, 129.

White Oak.—(Constituents) Johansen, Arch. d. Pharm., 209, 1876, 210 and A.J.P., 40, 1877, 453; Anon., Ph. Jl., [3], 2, 1871, 537; Kraemer, A.J.P., 62, 1890, 236.

Red Rose.—(Cultivation) Ellmer, C.A., 25, 1931, 1331. (Constituents) Cartier, Jl. de Ph., 7, 1821, 531; Peacock, Proc. P.Ph.A., 45, 1920, 162; Petrie, C.A., 19, 1925, 1000; Karrer and Schwarz, C.A., 23, 1929, 863.

Pale Rose.—Peacock, Proc. P.Ph.A., 46, 1921, 131.

Nutgall.—(History) Nierenstein, C.A., 26, 1932, 1164. (Source) Cook, Science, 57, 1923, 6. (Constituents) Guibourt, A.J.P., 16, 1844, 237; Anon., Ph. Jl., [3], 2, 1872, 614; Stenhouse, Ph. Jl., [2], 3, 1861, 330; Robiquet, Jl. de. Ph., 23, 1853, 241.

Gambir.—(Constituents) Trimble, A.J.P., 36, 1888, 99; Anon., Ph. Jl., [3], 2, 1872, 616; Lowe, A.J.P., 45, 1873, 447; Etti, A., 186, 1877, 327; Neubauer, A.J.P., 28, 1856, 329.

Kino.—(Constituents) White, Ph. Jl., 70, 1903, 676 and 71, 1903, 702; Henning, A.J.P., 25, 1853, 545; Etti, B., 17, 1884, 2241.

CHAPTER XLVI

AROMATIC HYDROCARBONS CONTAINING EIGHT, NINE, AND TEN CARBON ATOMS

THE hydrocarbons of the series C_nH_{2n-6}, containing eight carbon atoms, have the empiric formula,

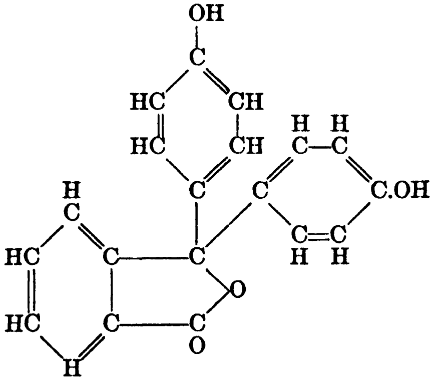
$$C_8H_{10}$$
$$C_n = C_8$$
$$H_{2n-6} = H_{2\times 8} = 16. \quad 16 - 6 = 10. \quad \text{Hence } H_{10}$$

This formula includes the three forms of dimethyl-benzene, $C_6H_4(CH_3)_2$, that is, ortho-, meta-, and para-xylenes, and also ethyl benzene, $C_6H_5C_2H_5$. From the three xylenes are derived the three forms of *phthalic acid,* $C_6H_4(COOH)_2$, which are mentioned in passing because the anhydride of the ortho-acid in condensation with phenol yields *phenolphthalein.*

PHENOLPHTHALEINUM—Phenolphthalein

(Phenolphthal.)

$C_{20}H_{14}O_4$



Molecular weight, 318.11

Summarized Description.

White or faintly yellowish-white, crystalline powder; soluble in about 10 parts of alcohol and in about 50 parts of ether; almost insoluble in water; melts at not less than 258° C.; dissolves in solutions of alkaline hydroxides and carbonates to a red fluid; such solutions are decolorized by addition of acids. For details, see U.S.P., p. 286.

For *tests for identity* and for *impurities* (fluorane, heavy metals and arsenic), see U.S.P., p. 287.

Remarks.—This chemical is made by condensing 1 molecule of phthalic acid anhydride with 2 molecules of phenol; sulfuric acid being used as the condensation agent.

Medical Properties.—Phenolphthalein has, of late years, become a highly popular purgative. It is the main constituent of such proprietaries as *probilin, phenolax* and *ex-lax.*

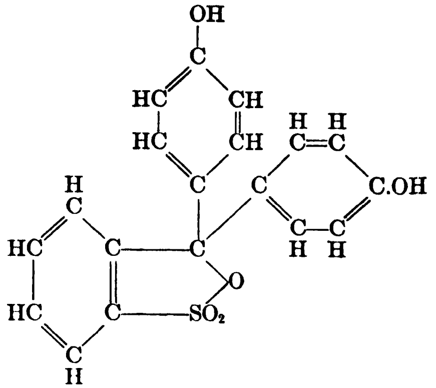
Incompatibilities.—See prescription No. 75 in Chapter LIX.

Dose.—60 mg. (1 grain).

PHENOLSULFONPHTHALEINUM—Phenolsulfonphthalein

(Phenolsulfonphthal.—Phenol Red)

$C_{19}H_{14}O_5S$



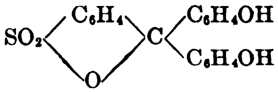
Molecular weight, 354.17

Summarized Description.

Bright to dark red powder; soluble in about 1300 parts of water and in about 290 parts of alcohol; soluble in acetone; insoluble in chloroform and ether; dissolves in solutions of alkaline hydroxides and carbonates to a red fluid; such solutions are turned to yellow by addition of acids. For details, see U.S.P., p. 287.

For *tests for identity* and for *impurity* (arsenic), see U.S.P., p. 288.

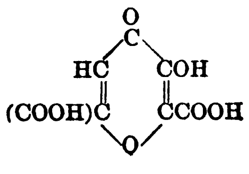
Remarks.—This chemical is made by the condensation of phenol with the anhydride of sulfobenzoic acid.



Medical Properties.—It is now largely used as a diagnostic reagent, in determining the functional activity of the kidneys. A sterile aqueous solution containing 6 mg. of the sodium salt in enough water to make 1 cc. is injected into the patient either intramuscularly or hypodermically and after two hours the urine voided by the patient during that period is tested colorimetrically against a standard solution of the chemical. When the kidneys are functioning properly, 65 to 80 per cent of the phenolsulfonphthalein will be eliminated within two hours.

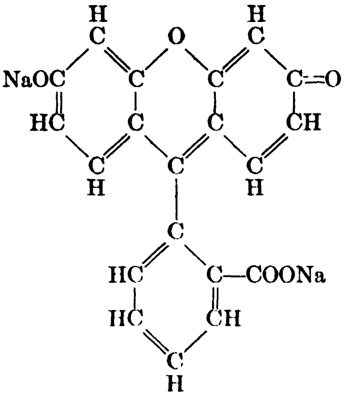
Diethylphthalate, $C_6H_4(COOC_2H_5)_2$, is made by heating phthalic acid with alcohol, using sulfuric acid or some other catalyst. It is an oily liquid, boiling at 302° C. at 760 mm. and at 295° C. at 734 mm. It is now largely used as a denaturant for alcohol used in the perfumery industry and has been used alone as a solvent for nonalcoholic perfumes.

Meconic Acid, $C_7H_4O_7$, a constituent of opium, is supposed to have the formula:



FLUORESCEINUM SOLUBILE—Soluble Fluorescein

(Fluoresc. Sol.—Fluorescein Sodium, Resorcinolphthalein Sodium)



$C_{20}H_{10}O_5Na_2$ Molecular weight, 376.07

The disodium salt of fluorescein.

Summarized Description.

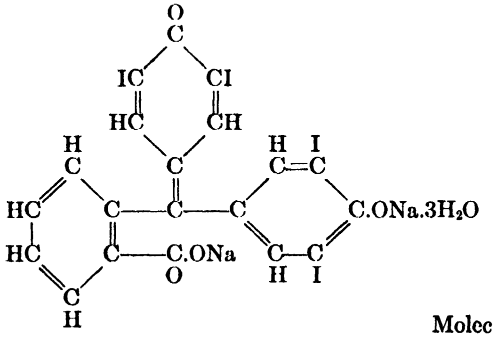
Orange-red powder; odorless and almost tasteless; freely soluble in water; sparingly soluble in alcohol. For details, see U.S.P., p. 175.

For *tests for identity* and for *impurities* (acriflavine, zinc, chloride, sulfate), see U.S.P., p. 175.

Remarks.—This new official is the disodium salt of the important dye, fluorescein. It is closely related to phenolphthalein. Soluble fluorescein is used for the diagnosis of corneal lesions and in the detection of minute foreign bodies embedded in the cornea.

IODOPHTHALEINUM SOLUBILE—Soluble Iodophthalein

(Sol. Iodophthal.—Tetraiodophenolphthalein Sodium, Tetraiodophthalein Sodium, Tetiothalein Sodium)



$C_{20}H_8O_4I_4Na_2.3H_2O$ Molecular weight, 919.78

The disodium salt of tetraiodophenolphthalein. It contains not less than 85 per cent of tetraiodophenolphthalein. The separated tetraiodophenolphthalein contains not less than 60 per cent and not more than 63 per cent of I.

Storage.—Preserve in well-closed containers.

Summarized Description.

Pale blue or blue violet crystalline powder; odorless, saline, astringent taste; decomposes on exposure to air; soluble in 7 parts of water; slightly soluble in alcohol. For details, see U.S.P., p. 195.

For ***tests for identity*** and for ***assay***, see U.S.P., p. 196.

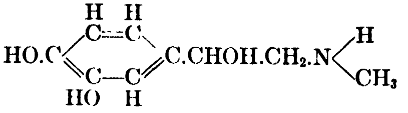
Remarks.—This new official is the sodium salt of the dibasic dye, tetraiodophenolphthalein. It is sometimes called *iodeikon.* It is used for the *x*-ray examination of the gallbladder.

Dose.—For each 10 kilograms of body weight: oral, 0.5 Gm. (8 grains); intravenous, 0.3 Gm. (5 grains).

EPINEPHRINA—Epinephrine

(Epineph.)

$C_9H_{13}O_3N$



Molecular weight, 183.11

Lævo-methylaminoethanolcatechol.

Storage.—Preserve in air-tight containers and protected from light.

Summarized Description.

White or light brown powder, darkens on exposure; odorless; very slightly soluble in water and in alcohol; insoluble in ether, chloroform, acetone and in fixed and volatile oils; soluble in dilute acids, forming salts. For details, see U.S.P., p. 146.

For *tests for identity,* see U.S.P., p. 146.

Remarks.—This chemical which is marketed under such names as *adrenalin, adrin,* etc., is a derivative of ethyl benzene, $C_6H_5CH_2CH_3$. It is obtained from suprarenal glands (p. 965) and possesses the property of constricting the blood vessels, making it of value in hemorrhage and in catarrhal conditions. It is now made synthetically. A *solution of epinephrine hydrochloride* is also official.

Dose.—0.5 mg. (1/120 grain).

LIQUOR EPINEPHRINÆ HYDROCHLORIDI—Solution of Epinephrine Hydrochloride

(Liq. Epineph. Hydrochlor.)

Solution of Epinephrine Hydrochloride is a solution of epinephrine in distilled water and hydrochloric acid, containing, in each 100 cc., not less than 0.095 Gm. and not more than 0.105 Gm. of $C_9H_{13}O_3N$.

Solution of Epinephrine Hydrochloride, diluted with physiological solution of sodium chloride in the proportion of 1 part of the Solution of Epinephrine Hydrochloride to 99 parts of the salt solution, and injected intravenously into a dog by the method described below, produces a rise in the systolic blood pressure of the dog corresponding to that produced by an equal amount of the standard solution of epinephrine hydrochloride prepared as directed below.

Storage.—Preserve in small, well-filled, amber-colored bottles or in ampuls.

Summarized Description.

Nearly colorless, slightly acid liquid; turns dark on exposure to air and light.

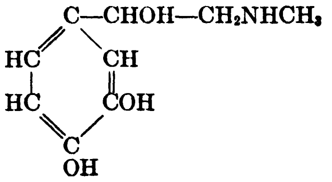
For *test for identity* and for *assay,* see U.S.P., p. 207.

Remarks.—Dried suprarenal glands of U.S.P. IX are no longer official; being replaced by the active principle, epinephrine (described above) and solution of epinephrine hydrochloride. The official solution contains 1/10 of 1 per cent of epinephrine and is assayed biologically.

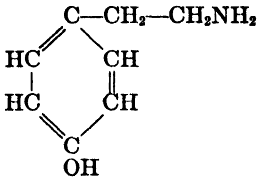
Dose.—Hypodermic, 1/2 cc. (8 minims).

Phenylaminoethanol Sulfate, N.N.R., is a synthetic alkaloid that has been recently introduced into American medicine. Its physiological relationship to epinephrine, tyramine (p. 941) and ephedrine (p. 932) can best be shown by the following structural formulæ:

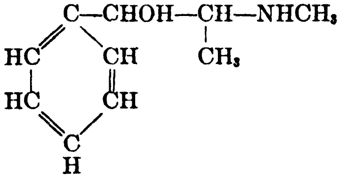
Epinephrine



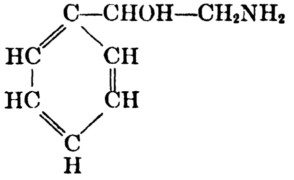
Tyramine



Ephedrine



Phenylaminoethanol



Synephrin, or *Paramethylaminoethanol-phenol hydrochloride,* is a synthetic closely resembling those described above.

Among the hydrocarbons of this series containing nine carbon atoms are the three trimethyl benzenes, $C_6H_3(CH_3)_3$, of which the most important is the symmetric form, *mesitylene;* the three methyl-ethyl benzenes, $C_6H_4\begin{matrix} \diagup CH_3 \\ \diagdown C_2H_5 \end{matrix}$; and the two propyl benzenes, $C_6H_5C_3H_7$, of which the most important is the isopropyl form, *cumene,* $C_6H_5{-}CH\begin{matrix} \diagup CH_3 \\ \diagdown CH_3 \end{matrix}$.

Of far greater importance in pharmacy are the unsaturated hydrocarbons of this series, *allyl benzene,* $C_6H_5CH{=}CH{-}CH_3$, and *iso-allyl benzene,* $C_6H_5CH_2CH{=}CH_2$. Neither of these bodies in themselves are of pharmaceutic interest, but each furnishes a long line of derivatives, many of which are constituents of volatile oils. Thus the alcohol of allyl benzene is *cinnamic alcohol,* $C_6H_5CH{=}CHCH_2OH$, and this on oxidation yields *cinnamic aldehyde,* $C_6H_5CH{=}CHCHO$, and *cinnamic acid,* C_6H_5-$CH{=}CHCOOH$.

The following derivatives of allyl benzene and iso-allyl benzene are of pharmaceutic importance:

Cinnamic alcohol.
Cinnamic aldehyde, U.S.P. VIII.
Cinnamic acid.
Coumaric acid.
Coumarin, N.F.

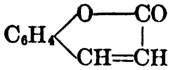
Anethol, N.F.
Eugenol, U.S.P.
Safrol, U.S.P. VIII.
Apiol.

Cinnaldehydum (U.S.P. VIII), or *Cinnamic Aldehyde,* is the aldehyde obtained from oil of cinnamon (p. 845). It can also be made synthetically as suggested above. Like oil of cinnamon, it is used as a carminative. Dose, 1 minim.

Both cinnamic aldehyde and cinnamic acid are found in nature elsewhere than in oil of cinnamon; that class of drugs called *balsams* being oleoresins containing benzoic and cinnamic acids, and usually some traces of the corresponding aldehydes.

Cinnamic acid is a crystalline solid of agreeable aromatic odor, and can be converted into oxycinnamic acid (*coumaric acid*), $C_6H_4\begin{matrix} \diagup OH \\ \diagdown CH{=}CHCOOH \end{matrix}$. When coumaric acid is treated with acetic acid anhydride a molecule of water separates, with the formation of coumarin.

Coumarin (N.F.) is the anhydride of ortho-oxycinnamic acid. Its graphic formula is

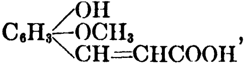


Coumarin was so named because first obtained from the Tonka bean, the fruit of *Dipteryx odorata* (formerly called *Coumarouna odorata*).

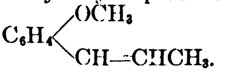
The synthesis of coumarin from coumaric acid was accomplished by Tiemann in 1877, and at present almost all the coumarin in commerce is made artificially.

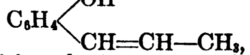
Coumarin is also found in the aromatic herbs, such as deer's tongue (*Liatris odorissima*) and mellilot (*Mellilotus alba*). There are also traces in the ordinary grasses, but more is produced by enzymic, glucosidal hydrolysis (see p. 713) upon drying, producing the odor of new-mown hay.

Coumarin occurs in white crystals, melting at 67° C., soluble in 14 parts of alcohol, and sparingly soluble in water. It is used for flavoring the cheaper grade of vanilla extracts.

Among other derivatives of allyl-benzene we find: *Ferulaic acid* (methyl-oxy-cinnamic acid),  $C_6H_3{<}\begin{matrix}OH\\OCH_3\\CH{=}CHCOOH\end{matrix}$, the chief constituent of the resin of asafetida (p. 876).

Caffeic acid, or *Dioxycinnamic Acid,* is a hydrolysis product of chlorogenic acid (see p. 811).

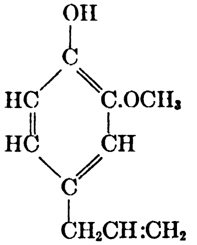
Anethol (parapropenyl-anisol), formula,  $C_6H_4{<}\begin{matrix}OCH_3\\CH{-}CHCH_3\end{matrix}$.

This body is the methyl ether of the phenol of allyl benzene,  $C_6H_4{<}\begin{matrix}OH\\CH{=}CH{-}CH_3\end{matrix}$, and is the chief constituent of the oils of anise, star anise, and fennel. It is a crystalline solid, melting at 21° C.

Three derivatives of iso-allyl benzene ($C_6H_5CH_2CH{=}CH_2$), eugenol, safrol, and apiol, are worthy of notice.

EUGENOL—Eugenol

$C_{10}H_{12}O_2$



Molecular weight, 164.09

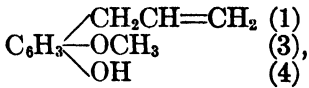
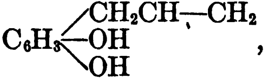
Eugenol is a phenol obtained from oil of clove and from other sources.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless or pale yellow, strongly refractive, thin liquid; aromatic odor of clove; pungent, spicy taste; darkens and becomes thicker on exposure to air; sp. gr. 1.066 to 1.070; miscible with alcohol, chloroform and ether; soluble in 2 volumes of 70 per cent alcohol; boils between 250° and 255° C.; optically inactive. For details, see U.S.P., p. 152.

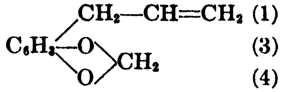
For *tests for identity* and for *impurities* (phenol, hydrocarbons), see U.S.P., p. 152.

Remarks.—Eugenol is allyl guaiacol,  $C_6H_3{<}\begin{matrix}CH_2CH{=}CH_2 & (1)\\OCH_3 & (3)\\OH & (4)\end{matrix}$, or the methyl ether of the dihydric phenol from iso-allyl benzene,  $C_6H_3{<}\begin{matrix}CH_2CH{-}CH_2\\OH\\OH\end{matrix}$, and is the chief constituent of the oil of cloves. It is an aromatic oily liquid, boiling at about 250° C.

Its conversion into vanillin has been already described (p. 805). Its medical properties are similar to oil of cloves, from which it is derived.

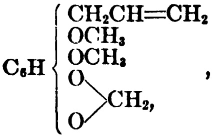
Dose.—0.1 cc. (1½ minims).

Safrolum (U.S.P. VIII), or *Safrol,* is allyl pyrocatechin-methylene ether,



$$C_6H_3\begin{cases}CH_2-CH=CH_2 & (1)\\ -O\diagdown & (3)\\ \quad\;\; >CH_2 & \\ -O\diagup & (4)\end{cases}$$

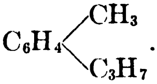
and represents eugenol with its methyl group replaced by the methylene group $\left(\begin{smallmatrix}-O\\ -C\end{smallmatrix}>CH_2\right)$. It is the chief constituent of oil of sassafras, and is a crystalline solid, melting at 8.5° C. and boiling at 233° C. Its medical properties are similar to oil of sassafras, after which it is named.

Apiol, 

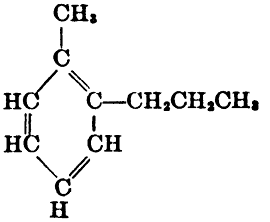
$$C_6H\begin{cases}CH_2CH=CH_2\\ OCH_3\\ OCH_3\\ O\diagdown\\ \quad >CH_2,\\ O\diagup\end{cases}$$

, is safrol, with two hydrogen atoms of its benzene nucleus replaced by (OCH_3) groups. It is a constituent of parsley fruit, and is a crystalline solid, melting at 30° C. Commercial apiol, highly esteemed by French physicians as an emmenagogue, is said to be the oleoresin of parsley fruit. This oleoresin and the drug from which it is derived were official in U.S.P. IX.

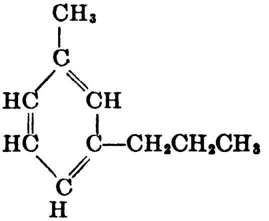
Several hydrocarbons having the formula $C_{10}H_{14}$ are known. The simplest of these are the methyl-propyl benzenes, $C_6H_4\begin{smallmatrix}\diagup CH_3\\ \diagdown C_3H_7\end{smallmatrix}$. As all bi-derivatives of benzene are known in three modifications, ortho-, meta-, and para- (see p. 775), so we have ortho-, meta-, and para-methyl-propyl benzene, in which the propyl group is normal, viz.:



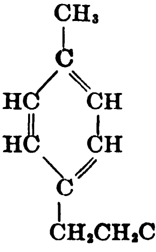
Ortho-



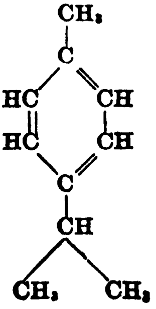
Meta-



Para-



More important than these, however, is the paramethyl-isopropyl benzene, or *cymene:*



This hydrocarbon, thus named because first found in oil of cumin (*Cuminum cyminum*), is made synthetically by treating parabrom-isopropyl benzene with methyl iodide in the presence of metallic sodium.

The graphic formula of cymene, given above, is proved correct by the synthesis just mentioned, and also by its behavior under various oxidizing agents.

Under certain conditions of oxidation it can be changed to para-toluic acid,

$C_6H_4{<}\begin{matrix}CH_3\\COOH\end{matrix}$; to terephthalic acid, $C_6H_4(COOH)_2$, or to cuminic acid,

$$C_6H_4{<}\begin{matrix}COOH & (1)\\CH(CH_3)_2 & (4).\end{matrix}$$

It will be noted that in the first-named acid the propyl group is oxidized to the carboxyl group; in the third-named acid it is the methyl group that is converted into the carboxyl, the isopropyl group remaining; while in the second acid both methyl and propyl groups are changed to carboxyl groups. Since all three acids have the groups attached to the benzene nucleus in the para-position, that must be the position of the methyl and propyl groups in the cymene.

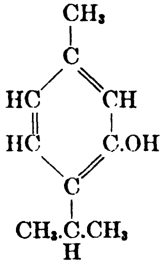
Cymene is of little practical importance in pharmacy, but it is of interest as a constituent of several volatile oils, notably the oils from the various species of thyme.

The following cymene derivatives or analogues are of pharmaceutic importance:

Thymol, U.S.P.
Chlorothymol, N.F.
Thymol iodide, U.S.P.
Carvacrol.
Carvone.

THYMOL—Thymol

$C_{10}H_{14}O$



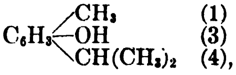
Molecular weight, 150.11

Summarized Description.

Large, colorless, translucent, rhombic prisms; aromatic thymelike odor; pungent aromatic taste; soluble in about 1000 parts of water and in about 0.8 part of alcohol; also soluble in chloroform, ether, olive oil, glacial acetic acid, fixed and volatile oils; when solid, heavier than water; when fused, lighter than water; melts between 48° and 51° C.; liquefies when triturated with camphor or menthol. For details, see U.S.P., p. 386.

For *tests for identity*, see U.S.P., p. 386.

Remarks.—Thymol is isopropyl-meta-cresol,



$$C_6H_3{<}\begin{matrix}CH_3 & (1)\\OH & (3)\\CH(CH_3)_2 & (4),\end{matrix}$$

or cymene with one hydrogen replaced by a hydroxyl group.

It occurs in several volatile oils; one of the most abundant sources being oil of horsemint. Thymol is obtained by saponifying oil of horsemint or oil of thyme, or a specific fraction of the same, with sodium hydroxide. The thymol sodium compound dissolves in the aqueous layer, which is separated from the oil portion, and the thymol set free by treating the aqueous layer with hydrochloric acid.

It is also made in the manner similar to the manufacture of menthol, that is, by submitting the oil to a freezing mixture and separating the stearopten (thymol) from the eleopten (p. 827) by means of a centrifugal apparatus. Another method of obtaining thymol is by the fractional distillation of the oils mentioned above. Of these three processes, the chemical treatment with sodium hydroxide is the one generally employed. Thymol has also been made synthetically from cumin aldehyde and from cymene.

Thymol affords an interesting illustration of crystallization by means of a nucleus. When obtained by the several methods just mentioned it is in the form of the thick liquid, and it is only when a crystal of thymol is introduced that the mass crystallizes. Thymol, when rubbed with some solid substance, such as chloral hydrate, menthol, and camphor, forms a thick liquid. A characteristic test for thymol is the blue-green color produced when a crystal of it is dissolved in glacial acetic acid and treated first with sulfuric acid, then with nitric acid.

Medical Properties.—An antiseptic, now largely used in the treatment of hookworm. When used for the latter purpose, purgative oils must not be given during the administration of the thymol, since oils hasten its absorption to such a degree that toxic symptoms result.

Dose.—As antiseptic, 125 mg. (2 grains), as anthelmintic, 2 Gm. (30 grains) per day.

THYMOLIS IODIDUM—Thymol Iodide

(Thymol. Iodid.)

Thymol Iodide is a mixture of iodine derivatives of thymol, principally dithymol-di-iodide [$(C_6H_2.CH_3.C_3H_7.OI)_2$], containing, when dried to constant weight over sulfuric acid, not less than 43 per cent of I.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Reddish-brown or reddish-yellow bulky powder; slight aromatic odor; insoluble in water or glycerin; slightly soluble in alcohol; quite soluble in chloroform, ether, collodion, fixed or volatile oils; not soluble in alkaline hydroxide solutions; not more than 1½ per cent of ash. For details, see U.S.P., p. 387.

For *tests for identity*, for *impurities* (halogens, alkalis, free iodine) and for *assay*, see U.S.P., p. 387.

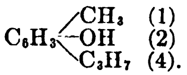
Remarks.—While this product, popularly known as *aristol*, was formerly considered as a definite chemical, it is now thought to be a mixture of several substances; one portion having a molecular weight of over 3000. Woollett even disputes the presence of dithymol-di-iodide in the mixture. It is made by dissolving 15 Gm. of thymol in 250 cc. of water with the aid of 20 Gm. of sodium hydroxide, then adding to this a solution of 6.35 Gm. of iodine and 8.3 Gm. of potassium iodide in 250 cc. of water. To the mixture add enough Labarraque's solution (650 to 700 cc. are necessary) to insure complete precipitation.

Aristol is a valuable iodoform substitute, containing the iodine in an easily assimilable form. From the standpoint of the iodine strength, however, it is inferior to both iodoform and iodol, for, as indicated by the formula, $C_{20}H_{24}O_2I_2$, it can contain only 46 per cent of iodine (being $^{252}/_{550}$ iodine). The pharmacopœial requirement is that it should contain at least 43 per cent of iodine and should yield not more than 1.5 per cent of ash.

Aristol is a useful antiseptic, possessing over the iodoform the great advantage of having an agreeable odor. Some care should be bestowed on the keeping of aristol, as it is found that it decomposes when subjected to strong light.

Chlorothymol (N.F. VI), or *Monochlorthymol*, $C_6H_2.CH_3.(OH).C_3H_7.Cl$, is a white crystalline granular powder that darkens to yellow or brown upon aging. It is soluble in less than one half its weight of alcohol and is almost insoluble in water. It is a more efficient antiseptic than is thymol and for this reason it is used in making *Liquor Antisepticus*, N.F. (p. 213).

Carvacrol.—An isomeric alcohol of thymol is carvacrol, isopropyl-ortho-cresol

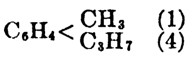


$$C_6H_3\begin{cases}CH_3 & (1)\\ OH & (2)\\ C_3H_7 & (4).\end{cases}$$

A comparison of this formula with that of thymol, given above, shows that the only difference is that in thymol the hydroxyl group is attached to carbon atom number 3 of the benzene nucleus, while in carvacrol it is attached to carbon atom number 2. In both substances the propyl group is of the "iso" variety.

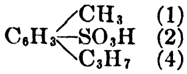
Carvacrol has been made synthetically from cymene by converting the latter (Formula I) into its sulfonic-acid derivative (Formula II), and on replacing the acid group by a hydroxyl group, carvacrol (Formula III) is obtained.

Formula I



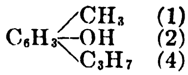
$$C_6H_4<\begin{matrix}CH_3 & (1)\\ C_3H_7 & (4)\end{matrix}$$

Formula II



$$C_6H_3\begin{cases}CH_3 & (1)\\ SO_3H & (2)\\ C_3H_7 & (4)\end{cases}$$

Formula III

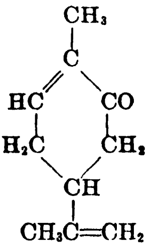


$$C_6H_3\begin{cases}CH_3 & (1)\\ OH & (2)\\ C_3H_7 & (4)\end{cases}$$

This body—a colorless, thick, acrid oil—is a constituent of certain volatile oils (origanum, etc.) and has been used as a thymol substitute in hookworm.

It was first prepared by heating carvone with glacial phosphoric acid, and because so obtained, and by reason of its acridity, it was called carvacrol.

Carvone.—



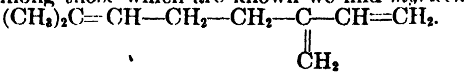
This body is a ketone, and is isomeric with carvacrol.

There are two forms of carvone, having the same graphic formula, but differing in that one deviates a ray of polarized light to the right, while the other turns it to the left. Dextrogyre carvone is the flavoring constituent of oil of caraway, *Carum carvi*, whence the name—carvone—is derived; while the levogyre form is a liquid of entirely different odor; that of oil of spearmint, of which it is the important constituent.

TERPENES

The terpenes are a series of hydrocarbons having the formula $C_{10}H_{16}$. While about twenty of these terpenes have been described, a much larger number is possible.

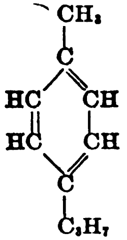
Thus we can imagine a series of chain compounds having the formula, $C_{10}H_{16}$, and among those which are known we find *myricene* the formula of which is supposed to be



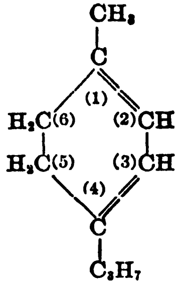
$$(CH_3)_2C{=}CH{-}CH_2{-}CH_2{-}\underset{\underset{CH_2}{\|}}{C}{-}CH{=}CH_2.$$

Again, we can have—what is generally the case—a body, $C_{10}H_{16}$, representing cymene, with one of its ethylene bonds loosened and with an atom of hydrogen attached to each of the free bonds, viz.:

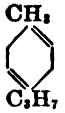
Cymene

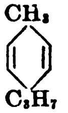


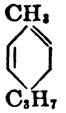
α-Terpinene

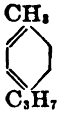


Since, as mentioned on p. 820, three cymenes each containing a normal propyl group are known (ortho-, meta-, and para-), so the closely similar terpenes may be found with their methyl and propyl groups in these three positions. Again, we can imagine a new line of terpenes, depending on whether the propyl group is normal or iso. Again, we can have four separate classes of terpenes dependent upon the relative position of the ethylene bonds found in the benzene nucleus, as shown in the following figures:

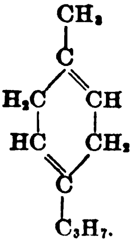








It is hardly necessary to state that the hexagons just given represent the benzene nucleus, with one double bond loosened. Thus, the first one is:



Beside all these combinations of $C_{10}H_{16}$, we can imagine each one of these compounds, containing asymmetric carbon atoms, existing in stereo-isomeric forms, and thus obtaining levogyre, dextrogyre, and inactive terpenes. Lastly, we can carry the isomeric possibilities still further by imagining terpenes containing, instead of methyl and propyl groups above given, two ethyl groups or one ethyl and two methyl groups.

The known terpenes are divided into the following systematic groups:

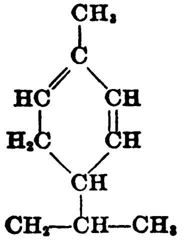
The Aliphatic Terpenes.—Each molecule of these terpenes absorbs six atoms of bromine, showing the presence of three ethylene groups. Two such terpenes are known, *myricene*, the formula of which is given on the preceding page, and which is found in the oil of bay, and *anhydrogeraniol*, which is found in the oil of geranium.

The Limonene Group.—In this group of terpenes each molecule absorbs four atoms of bromine, thereby showing the presence of two ethylene bonds.

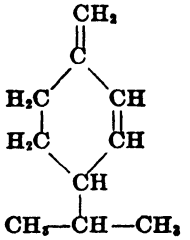
Among these terpenes we have the three *limonenes* (d, l, and i); *terpinolene*, an artificial terpene obtained by heating oil of turpentine with alcoholic sulphuric acid; *thujene* (or *tanacetene*), which is also artificially prepared, and *sylvestrene*, found in Swedish pine needle oil and its inactive isomere, *carvestrene*.

The Terpinene Group consists of two hydrocarbons, *terpinene* and *phellandrene*, the character of which is puzzling because of the difficulty in obtaining well crystallized bromine derivatives. It was formerly thought that neither would absorb bromine, but it is now known that each yields a dibromide. Wallach finds there are two types of phellandrene, the formulas of which are:

α-Phellandrene



β-Phellandrene



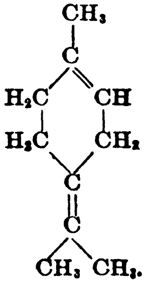
Among the terpenes belonging to this group we find *terpinene*, found in cardamom oil, dextrogyre *phellandrene*, from the oil of phellandrium, and levogyre phellandrene, found in the oil of *Eucalyptus amygdalina.*

The Pinene Group.—Each molecule of this group takes up two atoms of bromine, showing the presence of one ethylene bond. The known terpenes of this group are *pinenes*, two found in the oil of turpentine; *camphene*, found in oil of ginger, and made artificially by Berthelot (the only solid terpene known), *sabinene* found in sandalwood, and *fenchene*, which is an artificial terpene made indirectly from fenchyl alcohol.

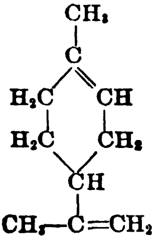
The difference between the different terpenes can best be studied by comparison of a few typical formulas.

Characteristic for the first group given above is the formula of myricene given on p. 823. Of the second group, the formulas ascribed to terpinolene and limonene are as follows:

Terpinolene

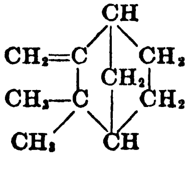


Limonene

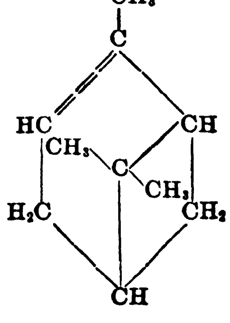


As mentioned above, the structure of the third group is a matter of doubt, while representatives of the pinene group are supposed to have the formulas given below:

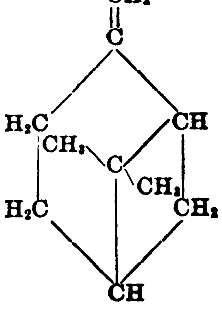
Camphene



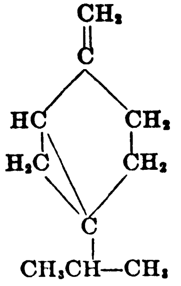
α- pinene



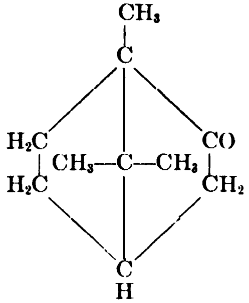
β- pinene

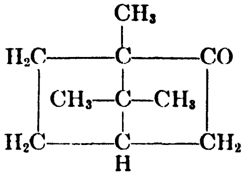


Sabinene



Formulas of this type are now being written upon a rectangular rather than a hexagonal figure. Thus the old and the new styles for the graphic formula of camphor (p. 831) are:





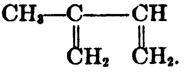
The transformation of one terpene into the other is a comparatively simple matter. Thus, on standing, limonene, found in the oil of lemon, is readily converted into pinene. This explains why the oil of lemon becomes terebinthinate.

Terpenes possess many striking chemical characteristics. For instance, those absorbing bromine generally give very beautiful crystalline bromo-compounds.

Another beautiful line of terpene derivatives are the nitroso-chlorides, such as limonene nitroso-chloride, $C_{10}H_{16}NOCl$, and these, on reduction, frequently yield well-crystallized oximes, such as carvoxime, $C_{10}H_{14}NOH$. Some terpenes are optically active, while others have no effect on the polarized ray of light. Those which do rotate the ray of light to the right or to the left always contain an asymmetric carbon atom (see p. 684).

Another point in the modern consideration of these derivatives is the contraction of the meaning of the word terpene. It was formerly applied to all the derivatives of cymene from $C_{10}H_{14}$ to $C_{10}H_{20}$. In modern chemical nomenclature bodies of the formula $C_{10}H_{16}$ are called terpadienes, while the word terpene is reserved for bodies of the formula $C_{10}H_{18}$, and the substances of the formula $C_{10}H_{20}$ are called terpanes. The application of the word terpene to $C_{10}H_{18}$ is unfortunate, since the word has for years been associated with bodies having the formula $C_{10}H_{16}$. Of the two classes last mentioned, terpenes represent the body $C_{10}H_{16}$, with one of their double bonds loosened and the bonds thus freed taken up with hydrogen atoms, making $C_{10}H_{18}$, while in the terpanes both double bonds are similarly loosened, and taken up by hydrogen, making $C_{10}H_{20}$.

Interesting modifications of the formula $C_{10}H_{16}$ are found in a group of hydrocarbons having the formula C_5H_8. These bodies are called *hemiterpenes;* literally, "half-terpene." An example of such a hemiterpene is *isoprene*, obtained by the distillation of rubber and supposed to have the formula



$$\mathrm{CH_3{-}\underset{\underset{CH_2}{\|}}{C}{-}\underset{\underset{CH_2.}{\|}}{CH}}$$

Again, we have bodies that are modifications of terpenes, containing half as much again carbon and hydrogen as terpenes, and, therefore, having the formula $C_{15}H_{24}$. This class of hydrocarbons are called *sesquiterpenes*. As examples of this may be cited *caryophyllene*, found in oil of cloves; *cadinene*, found in oil of cade; *celinene*, found in oil of celery seed; *santalene*, found in oil of sandalwood; and *zingiberene*, found in oil of ginger. Bodies having formula $C_{20}H_{32}$, $C_{36}H_{48}$, and $C_{40}H_{64}$ are also known.

The subject of terpenes serves as an introduction to that large class —the volatile oils. Practically all volatile oils are mixtures of many chemicals, and the old-fashioned classification of Dumas (1833) into terpenes, oxygenated products, oils containing nitrogen, and those containing sulfur, has long since become antiquated. For this reason the nitrogenated oils and those containing sulfur have already been considered under the appropriate grouping (oils of mustard, see p. 753; oil of bitter almond, see p. 793). Likewise, two other volatile oils that have no connection with the terpenes are the oil of sweet birch and the oil of wintergreen, which are esters of salicylic acid, and have been considered among the derivatives of the chemical. Nor is it wholly correct to consider the rest of the volatile oils merely as terpene derivatives. It is true, in the case of the larger number of them, that most of their bulk consists of terpenes, but it is also true that these oils owe very little of their character to the terpenes. Thus, while oil of lemon consists of about 94 per cent of the terpene, limonene, this is simply the solvent for the odorous principle, that consisting chiefly of *citral*. In fact, modern chemistry has attempted the problem of obtaining concentrated oils by removing the terpenes, and, in consequence, there is now on the market a large line of the so-called *terpeneless volatile oils*. In many cases these oils are not merely stronger than the natural oils, but are much better for general use. Thus, the terpeneless oil of lemon has, roughly speaking, sixteen times the flavoring power as has the oil of lemon, and possesses the great advantage of not becoming terebinthinate. A very good review of the fallacy of considering the terpenes, or even the terpene derivatives, as the most important constituents of the volatile oils, is found in the admirable paper of Professor Kremers, cited in the bibliography on page 838. This paper shows that the volatile oils contain a large number of different esters, aldehydes, alcohols, and ketones.

Two words of the obsolete nomenclature of the volatile oils still used in pharmacy are the terms *eleoptene* and *stearoptene*. These words were coined by Berzelius to represent respectively the liquid and solid portions of volatile oils. As mentioned above, most of the volatile oils are mixtures of quite a number of substances, and it so happens in some cases that some of these substances are solids dissolved in the liquid portion. These solid substances found in oils can sometimes be removed by chilling the oil in a freezing mixture and draining off the unfrozen eleoptene. Among the stearoptenes are found three official substances, camphor, menthol, and thymol. In modern chemistry the question as to whether the constituent of a volatile oil is solid or liquid is of but little importance, and the word stearoptene is not used in the Pharmacopœia.

Besides the official volatile oils containing terpenes, there are several terpene derivatives of interest to pharmacy which can be considered in a purely chemical sense. These are as follows:

Hydrocarbon:	Terebene, U S.P.
Monatomic alcohols:	Terpineol.
	Menthol, U.S.P.
	Borneol.
Diatomic alcohol:	Terpin hydrate, U.S.P.
Aldehyde:	Citral.
Ketone:	Camphor, U.S.P.
Dibasic acid:	Camphoric acid (U.S.P. VIII)
Inner oxide:	Eucalyptol, U.S.P.

TEREBENUM—Terebene

(Tereben.)

Terebene is a mixture of terpene hydrocarbons, chiefly dipentene and terpinene, prepared from oil of turpentine.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, thin liquid; agreeable thyme-like odor; aromatic terebinthinate taste; soluble in about 2.5 parts of alcohol; slightly soluble in water; resinified on exposure to light and air; sp. gr. 0.860 to 0.865; boils between 160° and 172° C. For details, see U.S.P., p. 380.

For *tests for identity* and for *impurities* (unaltered oil of turpentine, rosin), see U.S.P., p. 380.

Remarks.—Terebene is a mixture of several terpenes: among them, camphene, dipentene, cymene, and terpinene. Terebene is manufactured by treating 20 parts of oil of turpentine with 100 parts of concentrated sulfuric acid, and allowing the mixture to stand twenty-four hours. It is then heated to boiling, allowed to cool, when the oily layer on top is separated and neutralized with calcium carbonate and then distilled. The distilled terbene is rectified in order to secure a pure product.

Terebene in alcohol solution (1 : 500) is used as an antiseptic. It is also used in the concentrated form for bronchial troubles, for which purpose it is best given in the form of capsules. When administered for too long a time, however, it is apt to cause irritation of the stomach.

Dose.—¼ cc. (4 minims).

Terpineol, $C_{11}H_{17}OH$.—This unofficial chemical is made by the treatment of oil of turpentine with sulfuric acid and nitric acid. Several terpineols are known, three of them being solids and two viscid liquids. The crystalline terpineol is found in commerce, melts at 35° C., and was first obtained from the liquid terpineol by a method which afforded a striking illustration of the possibilities of crystallization. The liquid had been known to chemists, and many efforts have been made to secure its crystallization. All these attempts, such as freezing and the use of the nuclei, etc., have been in vain until Bouchardat and Voiry applied the idea of crystallization by analogy. These chemists had already prepared, from India rubber, a crystalline body having the formula $C_{10}H_{17}OH$, which they called caoutchin hydrate, and a minute crystal of this they dropped into liquid terpineol well cooled by use of a freezing mixture, and immediately the liquid terpineol began to crystallize, and in a short time five-sixths of the mass was solid. From that time the manufacture of crystalline terpineol has been simple, all that was necessary being to add to subsequent batches a few crystals of terpineol, such as originally produced by this brilliant experiment.

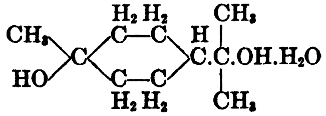
Terpineol is not used in medicine, but is largely used in perfumery as a basis of lilac perfumes; the substance in diluted form possesses an agreeable odor resembling that of the lilac blossoms. For perfumery purposes the viscid liquid terpineol, frequently marketed as "lilacin," is preferable to the crystalline.

Alpha terpineol is now obtained in large quantities from pine oil and is used on a large scale in the flotation process, mentioned on p. 594.

TERPINI HYDRAS—Terpin Hydrate

(Terp. Hyd.)

$C_{10}H_{20}O_2.H_2O$



Molecular weight, 190.17

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless, lustrous, efflorescent prisms or white powder slightly aromatic, somewhat bitter taste; soluble in about 200 parts of water and in about 10 parts of alcohol;

also soluble in chloroform, ether and boiling acetic acid; when heated slowly, it sublimes at 100° C.; when heated quickly, it melts between 115° and 117° C. For details, see U.S.P., p. 381.

For *tests for identity*, see U.S.P., p. 381.

Remarks.—Terpin hydrate is the crystalline hydrate of terpin, $C_{10}H_{18}(OH)_2$, which in turn can be considered as terpineol, with which 1 molecule of water has been combined or as a turpene from oil of turpentine (pinene, for example), to which 2 molecules of water have been added.

The water is, of course, added by chemical means—treatment with diluted mineral acids:

Oil turpentine (or its pinene)	$C_{10}H_{16}$
Add water	HOH
And we get terpineol	$C_{10}H_{17}OH$
Add another water	H OH
And we get terpin	$C_{10}H_{18}(OH)_2$

Terpin hydrate is generally manufactured by treating an alcoholic solution of oil of turpentine with nitric acid. The mixture is placed in a shallow porcelain dish for three or four days, when the crystals of terpin hydrate appear. The liquid is drained from the same, and the crystals are dried by pressing between sheets of filter paper. In order to obtain the pure product the substance is recrystallized. The yield of terpin hydrate by this process is about 12 per cent of the turpentine used.

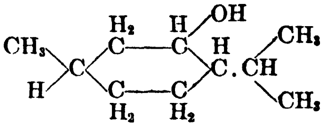
Terpin hydrate is used in chronic bronchitis and other troubles of the throat.

Dose.—250 mg. (4 grains).

Of late years an *elixir of terpin hydrate* has become quite popular as a cough remedy. Since the chemical does not dissolve in water, the preparation of an elixir which will contain 3 grains of terpin hydrate to the teaspoonful is a matter of some difficulty. In fact, about the only way to hold the terpin hydrate in solution is by making the preparation strongly alcoholic. A satisfactory recipe for the elixir is found in the National Formulary (p. 230). It, however, contains about 1 grain of terpin hydrate to the teaspoonful. A recipe is also given in the National Formulary for *elixir of terpin hydrate and codeine* (p. 230).

MENTHOL—Menthol

$C_{11}H_{20}O$



Molecular weight, 156.16

An alcohol obtained from oil of peppermint or other mint oils or prepared synthetically.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

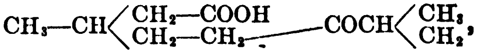
Summarized Description.

Colorless, acicular or prismatic crystals; strong odor of peppermint: warm aromatic taste, followed by sensation of cold when air is drawn into the mouth; slightly soluble in water; very soluble in alcohol, chloroform, ether, petroleum, benzin, liquid petrolatum, fixed and volatile oils; levorotatory; melts between 41° and 43° C.; liquefies when triturated with camphor, thymol, phenol or hydrated chloral. For details, see U.S.P., p. 231.

For *tests for identity* and for *impurities* (wax, paraffin, inorganic matter, thymol), see U.S.P., p. 231.

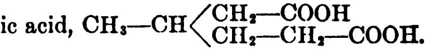
Remarks.—Menthol is an alcohol of the hydrocarbon, menthene, $C_{10}H_{18}$.

This formula is proved by the behavior of menthol when oxidized with potassium permanganate, when it yields oxymenthylic acid.



$$CH_3—CH\left\langle\begin{array}{l}CH_2—COOH\\CH_2—CH_2—\end{array}\right.——COCH\left\langle\begin{array}{l}CH_3\\CH_3\end{array}\right.$$

, and methyl-adipic acid,



$$CH_3—CH\left\langle\begin{array}{l}CH_2—COOH\\CH_2—CH_2—COOH.\end{array}\right.$$

That menthol is a secondary alcohol is shown by its oxidation by chromic acid into the ketone, methone, $C_{10}H_{18}O$.

As mentioned in the official definition, given above, menthol is an alcohol ("a stearopten having nature of a secondary alcohol," U.S.P. 1890), found in the oil of peppermint, and is obtained by placing the oil in a freezing mixture, when the menthol should crystallize out.

In the manufacture of menthol from the oil of peppermint the semisolid mass obtained by freezing is thrown on a filter paper, and after the greater portion of the liquid is drained, the crystals are dried by placing between folds of filter paper.

Menthol is now made synthetically in commercial quantities by the catalytic hydrogenation (p. 727) of menthone (from dementholized peppermint oil) and of pulegone (from pennyroyal oil). Originally only available in liquid form, solid synthetic menthol is now on the market.

The freezing process affords the test for the purity of oil of peppermint, and the Pharmacopœia of 1890 gave it among the tests. Unscrupulous distillers remove the menthol from the oil of peppermint and market the liquid part as oil of peppermint. Such an oil yields no menthol when chilled.

A pretty reaction identifying the menthol is the treatment of menthol with 50 per cent sulfuric acid, and boiling the mixture, when a blue coloration results.

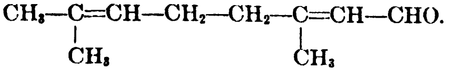
Menthol, like thymol, becomes liquid when triturated with an equal weight of camphor. Such a mixture, containing equal quantities of the two chemicals is recognized in the National Formulary under the name, *menthol camphoratum.* Menthol also liquefies when triturated with thymol, salol or chloral hydrate. (See prescription 75 in Chapter LIX.)

Menthol is used as a refrigerant. Its chief use, however, is as the constituent of antiseptic combinations, particularly those used for spraying in the nose. Another use for menthol is in the manufacture of the menthol pencils used for headache. Menthol rubbed on any part of the body evaporates, producing a chilling of the part, and thus involving a mild form of local anesthesia. It is also used in the form of an inhaler, this consisting of glass tubes plugged with cotton at either end, with intervening space loosely filled with menthol crystals, thus affording free access for the passage of air. When the air is sucked through this tube, a certain portion of the menthol volatilizes and enters the throat and nose, where it eventually condenses, thus bringing the healing antiseptic menthol in direct contact with the inflamed surface.

Dose.—60 mg. (1 grain).

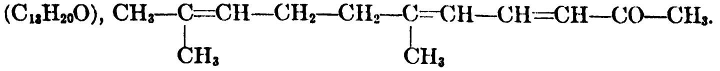
Citral (Geranial), $C_{10}H_{16}O$.—This aldehyde was isolated from oil of lemon in 1888, and found to be the flavoring principle of the oil. Semmler proved it to be identical with geranial, the aldehyde prepared by him by oxidation of geraniol. It is prepared from oil of lemon, which contains from 6 to 8 per cent of the chemical, and particularly from the lemon grass oils (*Andropogon citratus* and other species of *Andropogon*), which contain from 60 to 82 per cent, by formation of crystallization compound by treatment of the oil with sodium bisulfite. This compound, after washing with alcohol and ether, is treated with sodium carbonate, and the citral thus freed purified by distillation in vacuo.

As mentioned above, this body is the basis of terpeneless oil of lemon. Chemically, citral is supposed to be the aldehyde of the olefinic hydrocarbon, anhydrogeraniol, with formula:



$$CH_3-\underset{\underset{CH_3}{|}}{C}=CH-CH_2-CH_2-\underset{\underset{CH_3}{|}}{C}=CH-CHO.$$

On condensation of this body with acetone there is produced a ketone, pseudo-ionone,



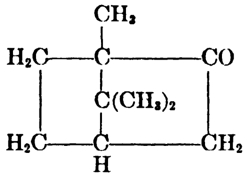
$$(C_{13}H_{20}O),\ CH_3-\underset{\underset{CH_3}{|}}{C}=CH-CH_2-CH_2-\underset{\underset{CH_3}{|}}{C}=CH-CH=CH-CO-CH_3.$$

This, on boiling with dilute sulfuric acid and trace of glycerin, yields an isomeric ring compound which is called *ionone*, and is of great commercial value as the basis of synthetic violet perfume. This is now known to consist of two isomeres, alpha-ionone and beta-ionone.

The real flavor of violet and of orris is still another isomere, called *irone*.

CAMPHORA—Camphor

$C_{11}H_{16}O$



Molecular weight, 152.12

A ketone obtained from *Cinnamomum Camphora* (Linné) Nees et Ebermaier (Fam. *Lauraceæ*) (Natural Camphor); or produced synthetically (Synthetic Camphor).

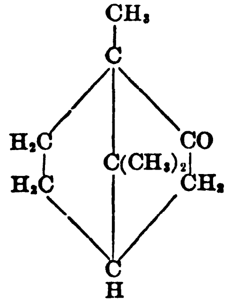
Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless, transparent crystals or white, translucent, volatile masses or granules, of tough consistence; characteristic odor; pungent aromatic taste; pulverizable by addition of alcohol, ether or chloroform; soluble in about 800 parts of water and in about 0.8 part of alcohol; also soluble in chloroform, ether, carbon disulfide, petroleum benzin, oil of turpentine, or in fixed or volatile oils; sp. gr. 0.990; melts between 174° and 177° C.; specific rotation $[\alpha]_D$, +41° to +42° in 200-mm. tube for natural camphor (for synthetic, +5° to −5°), in the proper alcoholic solution. For details, see U.S.P., p. 103.

For *tests for identity* and for *impurities* (chlorinated products), see U.S.P., p. 103.

Remarks.—While menthol is an alcohol, camphor, as noted above, is a ketone, the oxygen not being combined with hydrogen, but directly attached to a carbon atom.



Camphor has been prepared synthetically for a number of years, but only recently has it been able to compete with the natural product. In 1926 the United States imports of the two types of camphor were (*a*) natural, 3,600,000 pounds, (*b*) synthetic, 2,700,000 pounds. The use of synthetic camphor is permitted by U.S.P. XI. Synthetic camphor is usually made by treating pinene with hydrochloric acid and chromium trioxide.

As mentioned above, camphor is obtained from *Cinnamomum Camphora*, a handsome tree growing in Formosa. This tree is cut down, and the roots, trunk, and branches cut into small chips, placed in a rude retort containing heated water. When this water is boiled, the volatile products of the camphor wood distil over. The semisolid distillate is then submitted to hydraulic pressure, which removes all the eleoptene, the stearoptene remaining in the press. The manufacture of this substance affords an interesting and about the only illustration of a volatile oil containing so large a preponderance of the stearoptene as to be semisolid.

The liquid portion separated from the camphor by pressure is comparatively small in quantity, and is marketed under the name of *oil of camphor*, being in considerable demand in the Orient, although its consumption in this country is insignificant. It is well to bear in mind that this oil of camphor is not the familiar camphorated oil (liniment of camphor).

The crude camphor that is separated by expression is mixed with quicklime (to absorb water) and sublimed from a cast-iron retort into a cooled chamber, similar to that used in making flowers of sulfur. The camphor in this case condenses into a fine powder, which is then compressed into cakes.

As already mentioned on p. 138, the powdering of camphor is accomplished by the addition of a small quantity of alcohol, an example of pulverization by intervention. The powder thus obtained has the disadvantage of eventually forming again into a hard cake. Camphor, however, can be kept in the form of a permanent powder by triturating the powder, when freshly made, with a minute trace of white vaselin. Such powdered camphor, of course, would be unfit for preparing solutions, but for the usual purpose for which powdered camphor is employed, the addition of a minute quantity of the harmless substance, white vaselin, does not vitiate the camphor. When a lump of camphor, or powdered camphor free from oil, is placed in water, it floats on the surface, and then very rapidly moves to and fro on the surface of the water. This movement is produced by rapid evaporation of the camphor in contact with the water, and the sudden chilling of the water where the evaporation takes place, causing the movement in the direction where the water is warmer.

Camphor liquefies when triturated with menthol, thymol, chloral hydrate, salol, naphthol, and resorcinol; the liquefaction taking place in these cases is not supposed to be due to chemical change, but a mutual solution of the two solids, with the formation of a liquid. And that no chemical change is produced is shown by the fact that such a liquid, when poured into water, is rapidly separated into the two constituents. (See prescription No. 73 in Chapter LIX.)

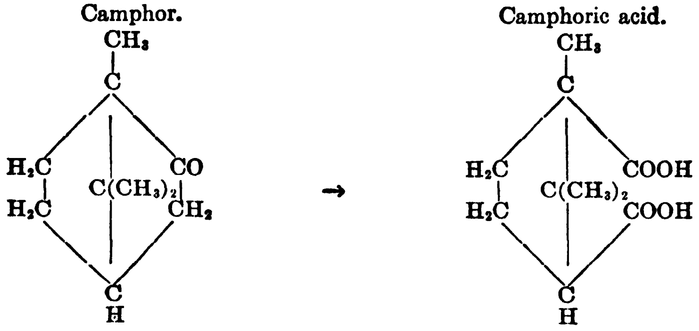
Such mixtures are said to be *eutectic*.

Camphor is a mild stimulant and is somewhat diaphoretic. It is used chiefly as anodyne, both internally and externally.

Dose.—By mouth or hypodermically, 200 mg. (3 grains).

Camphora Monobromata (N.F. VI) or *Monobromated Camphor*, $C_9H_{15}BrCO$, was discovered by Swarts in 1861, who prepared it by heating camphor and bromine for three hours in a sealed tube on a water-bath. It is generally made by the Maisch process, by mixing bromine and camphor in a retort, heating the mixture to 132° C., then cooling, and extracting the monobromated camphor with benzene. The substance thus obtained is purified by recrystallization. It occurs in colorless prismatic needles or in powder, is almost insoluble in water but is soluble in 5.2 parts of alcohol. It is used as a nervous sedative in 2-grain doses.

Acidum Camphoricum (U.S.P. VIII), or *Camphoric Acid*, is an oxidation product of camphor, nitric acid being the oxidizing agent employed. The oxidation from camphor to camphoric acid can be best explained by the following graphic formulas:

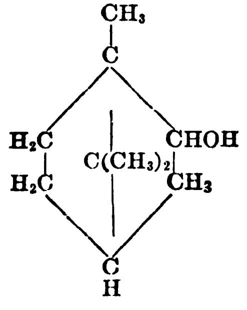

Camphor. → Camphoric acid.

In the description of camphoric acid given in the U.S.P. VIII, it was stated among other physical constants that it should in 10 per cent alcoholic solution possess the value $[\alpha]_D = 47.8$ degrees. This means that the specific rotating power of camphoric acid is 47.8 degrees—that is, when examined in a polariscope its solution, under ideal conditions, rotates the ray of light 47.8 degrees to the right.

To convert ordinary conditions of observation to the ideal, it is necessary to use as data in the calculation the observed angle of rotation, the length of the polariscope tube holding the liquid, and the strength of the solution employed. For details, see U.S.P. XI, pp. 459–461.

Camphoric acid is used as a stimulant as is camphor, but it is claimed to be less irritating. Dose 15 grains.

Borneol, $C_{10}H_{17}OH$.—This is a variety of camphor obtained from the plant, *Dryobalanops Camphora*, and is used quite largely in the east, although not employed in Europe and America. It can be made by treating camphor with sodium alcoholate, and investigations prove that it possesses the following graphic formula:

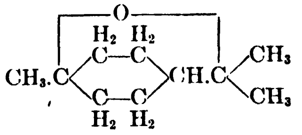


It differs from camphor in having two extra atoms of hydrogen and in being an alcohol, not a ketone.

EUCALYPTOL —Eucalyptol

(Cineol)

$C_{10}H_{18}O$



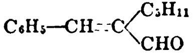
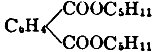
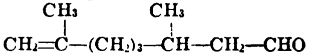
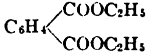
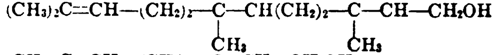
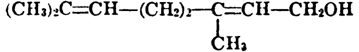
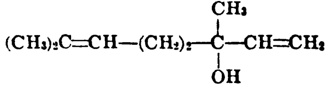
Molecular weight, 154.14

Eucalyptol is a substance obtained from oil of eucalyptus and from other sources.

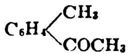
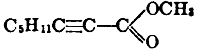
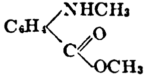
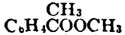
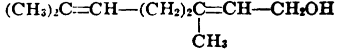
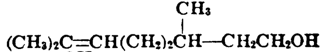
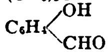
Summarized Description.

Colorless liquid; characteristic, aromatic camphoraceous odor; pungent, spicy taste; cooling to the mouth; very slightly soluble in water, miscible with alcohol, chloro-

PERFUMERY CHEMICALS

Name.	Synonym.	Formula.	Perfume uses.
Acetophenone		$C_6H_5OCH_3$	New-mown hay, syringa.
Alpha amyl cinnamic aldehyde	Jasmin aldehyde	 $C_6H_5{-}CH{=}C\begin{cases}C_5H_{11}\\CHO\end{cases}$	Jasmin.
Amyl benzoate		$C_5H_{11}C_7H_5O_2$	Fixative (p. 836). Solvent.
Amyl salicylate		$C_5H_{11}C_7H_5O_3$	Orchid, clover.
Amyl phthalate		 $C_6H_4\begin{cases}COOC_5H_{11}\\COOC_5H_{11}\end{cases}$	Fixative. Solvent.
Anisic aldehyde	Aubepine	$CH_3OC_6H_4CHO$	Hawthorn.
Benzophenone		$C_6H_5COC_6H_5$	Fixative.
Benzyl alcohol		(p 793)	Fixative. Solvent.
Benzyl acetate		$C_7H_7C_2H_3O_2$	Jasmin Ylang-ylang.
Benzyl benzoate		(p 797)	Fixative Solvent.
Benzylidene acetone		$C_6H_5CH{=}CH{-}CO{-}CH_3$	Lavender Soap perfume.
Bromostyrol		$C_6H_5CH{=}CHBr$	Hyacinth.
Cinnamyl alcohol		$C_6H_5CH{=}CHCH_2OH$	Rose. hyacinth.
Cinnamyl formate		$C_9H_9CHO_2$	Bergamot, rose.
Citronellal		 $CH_2{=}\overset{CH_3}{C}{-}(CH_2)_3{-}\overset{CH_3}{C}H{-}CH_2{-}CHO$	Geranium. Soap perfume.
Cresyl methyl ether		$CH_3{-}C_6H_5{-}OCH_3$	Cananga. Soap perfume.
Diphenyl methane		$CH_2(C_6H_5)_2$	Orange, geranium. Soap perfume.
Diphenyl ether	Phenyl oxide	$(C_6H_5)_2O$	Orange, geranium. Soap perfume.
Ethyl cinnamate		$C_2H_5C_9H_7O_2$	Fixative. Soap perfume.
Ethyl phthalate		 $C_6H_4\begin{cases}COOC_2H_5\\COOC_2H_5\end{cases}$	Fixative. Solvent.
Farnesol		 $(CH_3)_2C{=}CH{-}(CH_2)_2{-}\underset{CH_3}{C}{-}CH(CH_2)_2{-}\underset{CH_3}{C}{-}CH{-}CH_2OH$	Acacia, mignonette, lilac.
Geraniol		 $(CH_3)_2C{=}CH{-}(CH_2)_2{-}\underset{CH_3}{C}{=}CH{-}CH_2OH$	Soap perfume.
Geranyl acetate		$C_{10}H_{17}C_2H_3O_2$	Rose, neroli.
Geranyl benzoate		$C_{10}H_{17}C_7H_5O_2$	Bergamot, rose geranium.
Laurinic alcohol	Duodecyl alcohol	$CH_3(CH_2)_{10}CH_2OH$	Lily.
Linalool		 $(CH_3)_2C{=}CH{-}(CH_2)_2{-}\overset{CH_3}{\underset{OH}{C}}{-}CH{=}CH_2$	Rose.
Linalyl acetate		$C_{10}H_{17}C_2H_3O_2$	Lavender, bergamot, neroli.

PERFUMERY CHEMICALS—(*Continued*)

Name.	Synonym.	Formula.	Perfume uses.
Methyl acetophenone		 $C_6H_4\begin{cases}CH_3\\COCH_3\end{cases}$	New-mown hay.
Methyl anthranilate		$CH_3C_7H_6O_2N$	Neroli. Soap perfume.
Methyl benzoate	Oil of Niobe	$CH_3C_7H_5O_2$	"Peau d'Espagne."
Methyl heptine carbonate	Vert de Violette	 $C_5H_{11}C\equiv C—C\begin{cases}OCH_3\\=O\end{cases}$	Violet leaf
Methyl methyl anthranilate		 $C_6H_4\begin{cases}NHCH_3\\C\begin{cases}=O\\OCH_3\end{cases}\end{cases}$	Neroli
Methyl phenyl acetate		 $\overset{CH_3}{C_6H_4}COOCH_3$	Honey.
Nerol		 $(CH_3)_2C=CH—(CH_2)_2\underset{CH_3}{\underset{\vert}{C}}=CH—CH_2OH$	Rose, neroli.
Nerolin	Yara-yara	$C_{10}H_7OCH_3$	Neroli. Soap perfume.
Nonyl alcohol		$CH_3(CH_3)_7CH_2OH$	Rose
Nonyl aldehyde		$CH_3(CH_2)_7CHO$	Rose, neroli
Octine ethyl ether		$CH_3OCH_2(CH_2)_5C=CH$	Violet leaf.
Octyl alcohol		$CH_3(CH_2)_5CHOH—CH_3$	Rose.
Octyl aldehyde		$CH_3(CH_2)_6CHO$	Honey
Phenyl acetaldehyde		$C_6H_5CH_2CHO$	Hyacinth, lily of the valley.
Phenyl ethyl alcohol		$C_6H_5CH_2CH_2OH$	Rose, neroli.
Phenyl ethyl acetate		$C_6H_9C_2H_3O_2$	Floral bouquet, peach.
Phenyl propyl alcohol		$C_6H_5CH_2—CH_2—CH_2OH$	Hyacinth, jonquil, narcissus.
Rhodinol		 $(CH_3)_2C=CH(CH_2)_2\overset{CH_3}{\overset{\vert}{C}}H—CH_2CH_2OH$	Rose.
Salicyl aldehyde		 $C_6H_4\begin{cases}OH\\CHO\end{cases}$	Meadow-sweet.
Terpinyl acetate		$C_{10}H_{17}COOCH_3$	Lavender, bergamot.
Tridecyl aldehyde		$CH_3(CH_2)_{11}CHO$	"Odor modifier."

form, ether, glacial acetic acid, fixed and volatile oils; sp. gr. 0.921 to 0.923; boils between 174° and 177° C.; congeals at not less than 0° C. For details, see U.S.P., p. 151.

For *tests for identity* and for *impurities* (oil of eucalyptus, phenols), see U.S.P., p. 151.

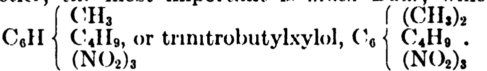
Remarks.—Eucalyptol was originally called *cineol*, because discovered in the oil of the seed of *Artemisia cinæ*, a variety of Levant wormseed. Eucalyptol is made synthetically by treatment of terpineol with phosphoric acid, and this synthesis suggests that eucalyptol is the anhydride of terpin.

Eucalyptol is prepared commercially by the fractional distillation of oil of eucalyptus; that portion of the oil distilling between 130° and 180° C. being collected and purified by redistillation over potassa. It is used as an antiseptic and stimulant.

Dose.—0.3 cc. (5 minims).

Artificial Musk.—Mention might here be made of the several chemicals, the odor of which so closely resembles that of musk that they can be used in perfumery in place of the natural product.

Of the many varieties, the most important is *musk Baur*, which consists either



of trinitrobutyltoluol, $C_6H\left\{\begin{matrix}CH_3\\C_4H_9\\(NO_2)_3\end{matrix}\right.$, or trinitrobutylxylol, $C_6\left\{\begin{matrix}(CH_3)_2\\C_4H_9\\(NO_2)_3\end{matrix}\right.$.

These are made by preparing the appropriate butyl compound by treating toluene or xylene with butyl bromide in the presence of aluminum chloride, and then treating the butyl compound with nitric acid.

Musk Baur occurs in white crystals, soluble in 200 parts alcohol, and this saturated alcoholic solution has perfume strength about equivalent to the 5 per cent tincture of musk of U.S.P. X.

Too much stress cannot be laid on the fact that the similarity in odor is purely accidental, and that under no circumstances can the artificial be used for the natural musk in medicine.

PERFUMES AND PERFUMERY CHEMICALS

There is no more fascinating branch of pharmaceutical practice than the blending of perfumes. Originally beginning with aromatized oils and unguents, then developing to aromatic tinctures and then to pomades and essences (p 840) the art of perfumery has now largely developed into the blending of perfumery chemicals, both natural and synthetic. Already we have discussed such perfumery chemicals as vanillin (p. 805), benzaldehyde (p. 7(3), heliotropin (p. 805), coumarin (p. 819), eugenol (p. 819), terpineol (p. 828), citral (p 830), musk (p. 836) and ionone (p. 831); in our next chapter we will consider the volatile oils; so at this place we will merely tabulate other chemicals, natural or synthetic, used in the manufacture of perfumes (see pp. 834, 835).

The only necessary comment on the foregoing table is to state that a *fixative* is a substance of heavy odor like musk, coumarin or heliotropin which is used in many perfume blends not because of its own odor but because it serves as a "background" to the more delicate perfumes that predominate in the blend.

Obviously a thorough discussion of the art of perfumery is beyond the limits of this book, but the reader will find in the Introduction a list of special books on perfumery. Among the modern fixatives may be cited methyl anthranilate, the methyl ester of methyl anthranilic acid, naphthol ether, benzyl cinnamate and betanaphthyl methyl ketone.

In closing the chapter it might be stated that chemists and physiologists are giving considerable attention to the relationship existing between the chemical structure of a substance and its odor. Some suggestive papers on this topic are found in the bibliography which follows this. The natural inference from researches on this subject is that synthetic odors may be prepared to meet definite requirements.

BIBLIOGRAPHY

Phenolphthalein.—(History) Baeyer, A., 183, 1876, 2. (Structure) Oddo, Gazz. ch. it., 44, I, 1914, 389; Consonno and Apostolo, C.A., 15, 1921, 2861. (Manufacture) Baeyer, A., 202, 1880, 36 and 68. (Properties) Utz, C.A., 15, 1921, 1235; Friedländer, B., 32, 1899, 575; Lund, Jl. Ch. Soc., 1930, 1844. (Uses) Drew, A.J.P., 50, 1878, 513. (Medical action) N.N.R., 1914, 206.

Phenolsulphonphthalein.—Remsen, Am. Ch. Jl., 6, 1884, 180.

Diethylphthalate.—Handy and Hoyt, Jl. A.Ph.A., 11, 1922, 928; 13, 1924, 600 and 702; 14, 1925, 219.

Epinephrine.—Takamini, A.J.P., 73, 1901, 523; Jowett, A.Ph.A., 52, 1904, 974; Abel, A.J.P., 75, 1903, 301; Hanzlik, Jl. A.M.A., 72, 1919, 577; Anon., C.A., 15, 1921, 3892; Funk and others, Jl. A.Ph.A., 12, 1923, 952. (History) Jowett, Ph. Era, 63, Aug. 14, 1926, 36. (Structure) Gordon, Jl. A.Ph.A., 17, 1928, 1195. (Medical Uses) Dragstedt, C.A., 23, 1929, 205. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1153.

Phenylamino-ethanol Sulphate.—Gordon, Jl. A.Ph.A., 17, 1928, 1195.

Mesitylene.—Fittig, A., 141, 1867, 129 and 147, 1868, 1.

Cumol.—Schotten and Baum, B., 17, 1884, 2551.

Cinnamic Alcohol.—Rugheimer, A., 172, 1874, 123.

Cinnamic Aldehyde.—(Preparation) Dumas and Peligot, A., 12, 1834, 24, 13, 1835, 76 and 14, 1835, 56. (Structure) Heusler, B., 17, 1884, 2117 and 24, 1891, 1805.

Cinnamic Acid.—Erlenmeyer, A., 137, 1866, 350; Stoddart, Jl. Ch. Soc., 1931, 1874.

Coumaric Acid.—(Synthesis and structure) Muller, A., 212, 1882, 122 and 150; Gabriel, B., 15, 1882, 2294 and A., 221, 1886, 266.

Coumarin.—(Source) Vogel (1820), through Thorpe Dict., 2, 1912, 157; Bourquelot and Herissey, Jl. ph. ch., 22, 1920, 289. (Synthesis) Perkin, Jl. Ch. Soc., 21, 1868, 53; Tiemann and Herzfield, B., 10, 1877, 287.

Caffeic Acid.—Dittmar, Jl. A.Ph.A., 12, 1923, 681.

Ferulaic Acid.—(History) Hlasiwetz and Barth, A., 138, 1866, 64. (Structure) Tiemann, B., 11, 1876, 650.

Anethol.—(Structure) Perkin, B., 10, 1877, 1604 and 2051. (Source) Dumas, Jl. de Ph., 19, 1833, 33.

Eugenol.—(Structure) Tiemann, B., 9, 1876, 418. (Preparation) Bonastre, Jl. de Ph., 13, 1827, 464; Erlenmeyer, A., 9, 1866, 95.

Safrol.—(Structure) Eijkmann, B., 18, 1885, R. 281. (Source) Binder, Rep. f. d. Ph., 11, 1821, 346; Grimaux and Ruotte, Comp. rend., 68, 1869, 928.

Apiol.—(Structure) Ciamician and Silber, B., 21, 1888, 913 and 1621; 22, 1889, 2481; 23, 1890, 2283; Thoms, B., 36, 1903, 1714. (Source) Homolle and Joret, Jl. de ph. et ch., 28, 1855, 212. (Oleoresin of parsley) Wolff, A.J.P., 49, 1877, 4; Walmsley, C.A., 23, 1929, 1470; Van Itallie, C.A., 26, 1932, 5336.

Cymene.—(Structure) Widmann, B., 24, 1891, 439, 970 and 1362. (Behavior) Widmann and Bladin, B., 19, 1886, 583; Schultz, B., 22, 1889, R. 452. (Source) Lallemand, A., 101, 1857, 119; 102, 1857, 117; Bruhl, B., 25, 1892, 150.

Thymol.—(Structure) Widmann, B., 15, 1882, 167; Fittica, A., 172, 1874, 305. (Sources) Arppe, A., 58, 1846, 41; Lallemand, A., 101, 1857, 119. (Synthesis) Anon., Jl. Soc. Ch. Ind., 42, 1923, 98. (Properties) Symes, Ph. Jl., [3], 9, 1879, 598; Maisch, A.J.P., 58, 1886, 51; Meldrum, Ch. News, 111, 1915, 193. (Medical uses) Livingston, C.A., 15, 1921, 2925; Caius, C.A., 18, 1924, 1338 and 1529; Docherty, C.A., 18, 1924, 124; Greene, Jl. A.Ph.A., 20, 1931, 20.

Thymol Iodide.—(History) Goldman, A.Ph.A., 38, 1890, 625. (Composition) Moles and Marquina, C.A., 13, 1919, 3156; Wollett, Jl. Am. Ch. Soc., 43, 1921, 553. (Manufacture) Beringer, A.J.P., 63, 1891, 175. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1156.

Carvacrol.—(Structure) Jacobsen, B., 11, 1878, 1060. (Synthesis) Reychler, B., 25, 1892, R. 208; Klages, B., 32, 1899, 1516; Wallach, A., 279, 1894, 369. (Source) Jahns, Arch. d. Pharm., 215, 1879, 1. (Medical uses) Livingston, C.A., 15, 1921, 2925.

Carvone.—(Structure) Wallach, A., 279, 1894, 369 and 305, 1899, 233. (Sources) Flückiger, B., 9, 1876, 47; Wallach, A., 277, 1893, 107. (Optical varieties) Baeyer, Arch. Pharm., 221, 1883, 283; Gladstone, Jl. Ch. Soc., 10, 1872, 1 and 25, 1887, 1.

Terpenes.—(General) Wallach, A., 24, 1891, 1524; Baeyer, B., 27, 1894, 436; Bennett and Holmes, Perf. Ess. Oil Rec., 9, 1918, 128; Challenger, Ind. Ch., 4, 1928, 315. (Anhydrogeraniol) Tiemann and Semmler, B., 28, 1895, 2126. (Para-menthadiene) Harries, A., 328, 1903, 322. (Myricene) Power and Kleber, Ph. Rund., 13, 1895, 61. (Limonene) Wallach, A., 239, 1887, 3 and 246, 1888, 222. (Terpinolene) Wallach, A., 227, 1884, 282 and 280, 1885, 272, Baeyer, B., 27, 1894, 436. (Thujene) Wallach, A., 350, 1906, 141; Kizhner, C.A., 6, 1912, 596. (Sylvestrene) Bertram and Walbaum., Arch. d.

Pharm., 231, 1893, 299. (Carvestrene) Baeyer, B., 27, 1894, 3485. (Terpinenes) Semmler, B., 34, 1901, 708; Weber, A., 238, 1887, 107; Wallach, A., 374, 1910, 224; Carter and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 543T. (Phellandrenes), Wallach, A., 336, 1904, 10 and 340, 1905, 10; Carter and co-workers, see above. (Camphene) Semmler, B., 42, 1909, 252; Bertram and Walbaum, Jl. prakt. Ch., [2], 49, 1894, 18. Berthelot, Comp. rend., 55, 1862, 496 and 544. (Limonene) Semmler, B., 28, 1895, 2143 and 33, 1900, 1455. (Pinenes) Wagner, B., 27, 1894, 2275; Wallach, A., 227, 1885, 300 and 363, 1908, 9; Shoppee and Simonsen, Jl. Soc. Ch. Ind., 48, 1929, 730; Faidutti, C.A., 24, 1930, 839; Armstrong, Jl. Soc. Ch. Ind., 51, 1932, 359. (Isodiprene) Aschan, C.A., 23, 1929, 127. (Dacrene) Blackie, Jl. Soc. Ch. Ind., 49, 1930, 26T. (Sabinene) Semmler, B., 35, 1902, 2045.

Terpene Nomenclature.—Baeyer, B., 27, 1894, 436; Kremers, Jl. A.Ph.A., 22, 1933, 227.

Hemiterpenes.—(Isoprene) Wendt, Ph. Zt., 52, 1907, 331; Pond, Jl. Am. Ch. Soc., 36, 1914, 165.

Sesquiterpenes.—(Caryophyllene) Wallach and Walker, A., 271, 1892, 285; Deussen, Loesche and Klemm, A., 369, 1909, 41. (Cadinene) Wallach, A., 271, 1892, 297. (Celinene) Semmler and Risse, B., 45, 1912, 3301. (Santalene) Semmler, B., 40, 1907, 1120. (Zingiberene) Soden and Rogalen, Ph. Zt., 45, 1900, 414.

Volatile Oils.—(General) Kremers, A.Ph.A., 46, 1898, 214. (Classification) Dumas, A., 6, 1833, 245; Berzelius, Lehrbuch der Chemie, 6, 1837, 580. (Antiseptic value) Martindale, Ph. Jl., 85, 1910, 668; Gilmour, A.Ph.A., 58, 1910, 293. (Terpeneless oils) Schimmel's Rep., Apr., 1893, 33 and 76; Parry, Ch. and Dr., 83, 1913, 378.

Terebene.—(Composition and manufacture) Power and Kleber, Ph. Rund., 12, 1894, 16.

Terpineol.—(Structure) Wallach, B., 28, 1895, 1773. (Properties) Bouchardat and Voiry, Comp. rend., 104, 1887, 996. (Uses) Teeple, Jl. Soc. Ch. Ind., 50, 1931, 327.

Terpin Hydrate.—(Structure) Baeyer, B., 26, 1893, 2865; Claus, C.A., 26, 1932, 127. (Manufacture) Wallach, A., 227, 1885, 284; Hahn, A.J.P., 59, 1897, 73; Austerweil, C.A., 19, 1925, 2653. (Uses) Lepine, Am. Dr., 15, 1886, 15. (Elixir) McClintock, A.J.P., 73, 1901, 31; Hain, Apothecary, 7, 1910, 20.

Menthol.—(History) Grove-Palmer, Jl. Soc. Ch. Ind., 50, 1931, 697. (Structure) Arth, B., 19, 1886, R., 436; Read, Jl. Soc. Ch. Ind., 46, 1927, 871; Wokes, Quart. Jl. Ph., 5, 1932, 233. (Sources) Anon., Jl. Soc. Ch. Ind., 44, 1925, 56. (Synthesis) Blagden, Br. Pat. 238314, 1924; Schimmel, C.A., 22, 1928, 4716; Horiuchi, C.A., 22, 1928, 3886; Jordan and co-workers, C.A., 23, 1929, 2191; Read and Grubb, Jl. Soc., Ch. Ind., 51, 1932, 331T. (Preparation) Todd, A.J.P., 58, 1886, 159. (Tests) Fritsche, A.Ph.A., 34, 1886, 541. (Properties) Kyle, A.Ph.A., 34, 1886, 541; Meldrum, Ch. News, 111, 1915, 229.

Citral.—(Structure and properties) Tiemann, B., 31, 1898, 3278, 3297 and 3324. (Sources) Dodge, Am. Ch. Jl., 11, 1889, 456 and 12, 1890, 563; Kremers, Dr. Circ., 59, 1915, 355.

Ionones and Irones.—Tiemann and Krueger, B., 26, 1893, 2675; Tiemann, B., 31, 1898, 808 and 867; Kraemer, A.J.P., 67, 1895, 346; Sadtler, A.J.P., 81, 1909, 181; Ruzicka, C.A., 13, 1919, 3180.

Camphor.—(Structure) Bredt, B.. 26, 1893, 3040; Kaul, C.A., 23, 1929, 4210. (Synthesis) Reychler, B., 29, 1896, 69; Semmler, B., 33, 1900, 3420; Pond, Jl. Soc. Ch. Ind., 26, 1907, 383. (Source) Rusby, Jl. Soc. Ch. Ind., 26, 1907, 380; Duncan, Harper's Magazine, 122, 1911, 381; Houseman, A.J.P., 87, 1915, 49; Anon., Yearbook, A.Ph.A., 6, 1917, 339; Anon., Pharm. Era, 51, 1918, 280 and 301 and 53, 1920, 235; Stockberger Jl. Soc. Ch. Ind., 41, 1922, 453R; Anon., *ibid.*, 43, 1924, 493; Yahagi, C.A., 23, 1929, 636; Sherwood and Short, Jl. Soc. Ch. Ind., 50, 1931, 697B. (Synthetic camphor) Lenz., Arch. d. Pharm., 249, 1911, 286; Dubosc, Am. Dr., 69, Oct., 1921, 44; Anon., Jl. Soc. Ch. Ind., 44, 1925, 977; Egger and Paillard, *ibid.*, 44, 1925, 148B; Bornemann, Ch. Zt., 54, 1930, 8 and 22. (Properties) LaWall, Merck's Rep., 19, 1910, 1; Matteuci, A.J.P., 6, 1839, 174; Rayleigh, Ch. and Dr., 36, 1890, 707; Leo and Rimbach, Jl. Soc. Ch. Ind., 38, 1919, 738A. (Powdering) Lowd, A.Ph.A., 19, 1871, 441; England, A.J.P., 50, 1887, 508. (Camphor chloral) Brown, A.Ph.A.. 22, 1874, 232. (Other liquefactions) Caille, Comp. rend., 148, 1910, 1458.

Oil of Camphor.—Lallemand, A.J.P., 32, 1860, 265; MacEwan, Ph. Jl., [3], 15, 1885, 1045; Rochussen, C.A., 17, 1923, 1635.

Monobromated Camphor.—Maisch, A.J.P., 44, 1872, 337.

Camphoric Acid.—(Structure) Bredt, B., 26, 1893, 3040. (Synthesis) Komppa, Jl. Ch. Soc., 99, 1911, 29. (Uses) Reichert, Ph. Jl., [3], 19, 1888, 507.

Borneol.—(Structure) Wagner, B., 32, 1809, 2324. (Source) Anon., Ph., Jl., [3], 12, 1881, 83. (Synthesis) Wallach, A., 230, 1885, 225.

Eucalyptol.—(Structure) Wallach, A., 258, 1890, 335 and 291, 1896, 350; Rupe, B., 33, 1900, 1129. (Synthesis) Wallach, A., 239, 1887, 21. (Sources) Wallach and Brass, A., 225, 1884, 291; Jahns, B., 17, 1884, 2941.

Synthetic Perfumes.—(Musk) Baur, B., 24, 1891, 2832; Moelting, C.A., 16, 1922, 989; Battegay and Kappeler, C.A., 19, 1925, 376; Delange, C.A., 22, 1928, 4721; Bogert, C.A., 23, 1929, 4953. (General) Brittain, Ch. and Dr., 85, 1914, 59; Umney, Perf. Ess. Oil Rec., 2, 1911, 134; Bennett and Hollins, Perf. Ess. Oil Rec., 9, 1918, 128; Bush, Pharm. Era, 53, 1920, 372; Hannemann, C.A., 18, 1924, 2480; Bolis, C.A., 18, 1924, 2578; Cerighelli, Jl. Soc. Ch. Ind., 44, 1925, 337B; Lewisohn, Jl. Soc. Ch. Ind., 44, 1925, 227B; Grignard and Escourrou, C.A., 19, 1925, 2635; Elge, C.A., 21, 1927, 299; Descollonges, C.A., 22, 1928, 3130; Romeo, C.A., 22, 1928, 4721; Redgrove, Am Perf., 24, 1930, 725 and 735; Hoejenbos and Coppens, Jl. Soc. Ch. Ind., 50, 1931, 863B and 51, 1932, 48B; Shepard and Leaper, C.A., 26, 1932, 3620; Anon., Ph. Jl., 130, 1933, 185.

Fixatives.—Clemonte, C.A., 22, 1928, 4721.

Physiology of Odors.—Teudt, C.A., 14, 1920, 1685; Furukawa, also Kodama, C.A., 15, 1921, 1145; Zwaardemaker, C.A., 16, 1922, 3666; Martincalderin, C.A., 17, 1923, 2733; Hopper, C.A., 18, 1924, 2721; Missenden, C.A., 20, 1926, 1494; Poucher, C.A., 22, 1928, 3259; Redgrove, C.A., 22, 1928, 3260; Dyson, C.A., 23, 1929, 853; Von Braun and co-workers, C.A., 24, 1930, 1341; Angeli, C.A., 25, 1931, 2434 and 4541; Anon., Ph. Jl., 127, 1931, 415.

CHAPTER XLVII

VOLATILE OILS AND VOLATILE OIL DRUGS

A LARGE number of volatile oils and drugs depending for their activity upon volatile oils are recognized by the Pharmacopœia, and these we will study in the following order:

I. Official volatile oils obtained from unofficial drugs.
II. Official drugs containing volatile oil.
III. Official drugs containing volatile oil and resin.
IV. Official drugs containing volatile oil and bitter principle.
V. Official oleoresins.
VI. Official balsams.

Official volatile oils not considered in the first group will be studied under the drug from whence they are derived.

OFFICIAL VOLATILE OILS OBTAINED FROM UNOFFICIAL DRUGS

The chemistry of volatile oils has been studied on p. 827 but before taking up the individual members of the group a few words as to the physical difference between fixed and volatile oils may be advisable. The general test for distinction—in fact, expressed in the names, "fixed," and "volatile"—was touched upon in discussing fixed oils (p. 728).

Drop some of the liquid on a piece of paper, and warm the stain over a lamp; if a volatile oil, the stain disappears; if a fixed oil, it remains.

A very homely test is the behavior of a glass stopper toward fixed and volatile oils. The ground-glass stopper of a bottle containing a fixed oil rotates easily and quietly in the neck, whereas a volatile oil stopper, when twisted in the neck, makes a squeaking noise under the operation.

The **separation of volatile oils** from their original sources varies according to the nature of oil, the character of the plant part whence derived, and other considerations. The methods can, however, be roughly classified into the following groups:

I. *Distillation with Water.*—In this case the drug is placed in a still with cold water, care being taken to prevent the drug from touching the bottom of the still, for if so exposed, the plant part is apt to scorch, thus affecting the odor of the distillate (p. 121). The water is then slowly and carefully heated, and as it distils it carries over with it the volatile oil found in the plant. This is the process by which most crude oils are distilled in their native home, especially those distilled in the Orient. Example, oil of cajuput.

II. *Distillation with Steam.*—This process has already been fully described (p. 121), hence it is merely necessary to say that it is employed in place of distillation with water by all progressive distillers of oils produced in Europe and America. This is the way that oil of peppermint is now obtained in Michigan.

III. *Distillation Alone.*—This process is applied in the case of some crude cheap oils, such as the manufacture of oil of turpentine from its oleoresin, which is placed in a still and cautiously heated until all the oil passes over. The residue in the still in the case considered constitutes official rosin. Even in the case of oil of turpentine, some distillers introduce a small stream of water into the distilling mass to lessen the danger of scorching.

IV. *Destructive Distillation.*—The so-called "oils" obtained by this process, which has already been described on p. 121, are in truth tarry products, and no longer classed among the true oils. An example of these is the official oil of cade.

V. *Vacuum Distillation.*—This process, described on p. 121, is practically never used in obtaining a crude oil from its plant sources, but is used largely in refining crude oils.

VI. *Expression.*—The oils from the rind of the fruits of the Citrus family—lemon, orange, bergamot, etc.—reside in the outer layer of cells, hence can be obtained by expression. This process is used in these cases because the distillation of the rind yields an inferior oil. The extraction of the oil is accomplished either by pressing the quarter or half fruit against a sponge, which is eventually expressed into the container, or by the use of a complicated machine which ruptures the oil cells by scraping, and then pressing the broken cells against sponges. This machine works well only with the round fruits, orange and bergamot, being useless in the case of lemon.

The *ecuelle à piquer* is a hollow bowl disk studded with needles on its concave side, and provided with a hollow handle which collects the oil separated from the rind by the pricking of needles when the instrument is revolved against the fruit. It is not used much at present.

VII. *Enfleurage.*—This method is employed in removing from flowers odors too subtle to stand distillation and too scarce to permit of expression. Briefly explained, the process consists of bringing the fresh flowers in contact with lard made odorless by prolonged washing with water. The lard is spread on glass plates in thin layers, and thereon are thrown the flowers, usually prevented from direct contact with the lard by having wire netting interposed. When the flowers wither, new ones are spread on the netting, and the batches are renewed until the lard has the sufficient amount of odor. Such odorous lard is called a *pomade,* the qualifying phrases *triple* and *quadruple* meaning that the lard has been impregnated with the odor of three or four times its weight of flowers respectively. The pomades are usually made direct into perfume by mixing the lard with cologne spirit (p. 657), which dissolves the perfume, but not the fat. The latter is then separated by filtration. The filtrate forms the perfumer's *extract,* the standard strength of which is the filtrate from a mixture of 1 Kg. of pomade and 1250 cc. cologne spirit. While the odorous principles of flowers are known to be volatile oils, only recently have efforts been made to isolate the oil, perfumers finding that the extracts above described answered their purpose. The volatile oil of jasmin has, however, been isolated by Verley by shaking the pomade with liquid petrolatum, which absorbs the oil, and extracting the latter from its petrolatum solution by shaking with acetone.

Trabaud (1930) reports on an improved method of enfleurage in which 1000 Kg. of fresh jasmin flowers yield 5 to 6 Kg. of a pomade, containing about 1.5 Kg. of pure floral oil.

VIII. *Percolation.*—Of late, perfume chemists have been extracting floral volatile oils more or less associated with solid fats by percolating the flowers with low-boiling solvents, such as methyl chloride. It is beyond the limits of this work to give more than this brief statement as to extraction of volatile oils, and for further details the reader is referred to the books on volatile oils and perfumes cited in the bibliography.

Oleum Cajuputi (U.S.P. X), or *Oil of Cajuput*, is distilled from fresh leaves and twigs of *Melaleuca Leucadendron* and rectified by steam distillation. It contains 55 per cent of cineol, a small quantity of terpenes, a solid terpineol, some aldehydes, etc. The green color of the oil has been said to be due to the copper absorbed from the still, but Spoelstra (1929) states that is due to azulene (p. 882). The oil is used as a stimulant and rubefacient. *Dose*, 0.5 cc. (8 minims).

OLEUM CHENOPODII—Oil of Chenopodium

Ol. Chenopod.—Oil of American Wormseed

Oil of Chenopodium is the volatile oil distilled with steam from the fresh, overground parts of the flowering and fruiting plant of *Chenopodium ambrosioides* var. *anthelminticum* (Linné) A. Gray (Fam. *Chenopodiaceæ*).

Oil of Chenopodium contains not less than 60 per cent and not more than 80 per cent of an acetic acid-soluble fraction.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

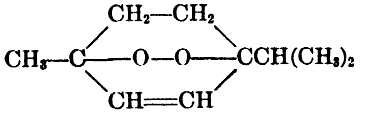
Summarized Description.

Colorless or pale yellow liquid; characteristic disagreeable odor and taste; soluble in 8 volumes of 70 per cent alcohol; refractive index, 1.4723 to 1.4790. For details, see U.S.P., p. 252.

For *tests for identity*, for *impurities* (heavy metals) and for *assay*, see U.S.P., p. 252.

Composition.—*Ascaridol* (60 per cent); four hydrocarbons (paracymene, terpinene, limonene and dihydroparacymene); butyric acid; methyl salicylate.

Ascaridol the active constituent is an unstable organic dioxide exploding when heated with mineral acids. It is supposed to have the formula:



Medical Properties.—Anthelmintic, of marked value in hookworm, usually administered mixed with castor oil. The oil is distinctly toxic, because of the ascaridol which it contains.

Dose.—1 cc. (15 minims).

Chenopodium, or *American Wormseed*, was official in the Pharmacopœia of 1890. Its only important constituent is the oil described above.

Oleum Erigerontis (U.S.P. VIII), or *Oil of Erigeron*, is distilled from the fresh flowering herbs of *Erigeron canadensis*. It contains dextrogyrate limonene and is used as a hemostatic and stimulant.

OLEUM JUNIPERI—Oil of Juniper

Ol. Junip.—Juniper Oil

Oil of Juniper is the volatile oil distilled with steam from the dried ripe fruit of *Juniperus communis* Linné (Fam. *Pinaceæ*).

Storage.—Preserve in well-filled bottles, in a cool place and protected from light.

Summarized Description.

Colorless, faintly green or yellow liquid; characteristic odor and taste; soluble in 4 volumes of alcohol; sp. gr. 0.854 to 0.879; optical rotation, 0 degree to −15 degrees in 100-mm. tube; refractive index, 1.4780 to 1.4840. For details, see U.S.P., p. 256.

Composition.—Pinene, cadinene, a terpineol, $C_{10}H_{17}OH$, borneol and isoborneol.

Medical Properties.—Stimulant, diuretic. *Gin* (p. 205) is an alcoholic solution of this oil prepared by distilling fermented juniper berries, and is simulated in the formerly official *compound of spirit of juniper* (p. 205).

Dose.—Of oil, 0.1 cc. (1½ minims).

Juniperus (U.S.P. VIII; N.F. VI) is the fruit of *Juniperus communis*. Beside the oil (about 1 per cent) the berries contain fruit acids, pectin, protein and resins. It is a popular domestic diuretic. *Dose*, 1 drachm.

OLEUM LAVANDULÆ—Oil of Lavender

(Ol. Lavand.—Oil of Lavender Flowers)

Oil of Lavender is the volatile oil distilled with steam from the fresh flowering tops of *Lavandula Spica* Linné (*Lavandula officinalis* Chaix, *Lavandula vera* DeCandolle) (Fam. *Labiatæ*). Oil of Lavender contains not less than 30 per cent of esters calculated as linalyl acetate ($C_{10}H_{17}.C_2H_3O_2$).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless or yellow liquid; characteristic odor and taste; soluble in 4 volumes of 70 per cent alcohol; sp. gr. 0.875 to 0.888; optical rotation, −3 degrees to −10 degrees in 100-mm. tube; refractive index, 1.4590 to 1.4640. For details, see U.S.P., p. 257.

For *tests for identity*, for *impurities* (alcohol, acetins) and for *ester assay*, see U.S.P., p. 257.

Composition.—Levogyrate linalyl acetate, 30 to 45 per cent; geraniol, some terpenes, etc.

Remarks.—*Oil of spike* is a crude oil of lavender made by distilling the lavender herb. Most of the oil of spike in the American market is a factitious product.

Medical Properties.—Stimulant. Used mostly as perfume. Official preparations: *Spirit of lavender* (p. 204) and *compound tincture of lavender* (p. 249). A constituent of *aromatic spirit of ammonia* (p. 506).

Dose.—0.1 cc. (1½ minims).

OLEUM ROSÆ—Oil of Rose

Ol. Rosa.—Otto of Rose)

Oil of Rose is the volatile oil distilled with steam from the fresh flowers of *Rosa gallica* Linné and *Rosa damascena* Miller, and varieties of these species (Fam. *Rosaceæ*).

Storage.—Preserve in well-stoppered, completely filled containers, in a cool place and protected from light.

Summarized Description.

Colorless or yellow liquid; characteristic odor and taste; on cooling changes to a translucent crystalline mass, which is easily liquefied on warming; sp. gr., 0.848 to 0.863; optical rotation, −1 degree to −4 degrees; refractive index, 1.457 to 1.463. For details, see U.S.P., p. 266.

For *tests for identity*, see U.S.P., p. 266.

Remarks.—This oil, recognized in U.S.P. VIII and earlier Pharmacopœias, is obtained from *Rosa gallica* and *Rosa damascena.* The former plant yields the French oil, while the latter is the source of the Bulgarian. It consists of a liquid portion containing geraniol (p. 830), 60 to 75 per cent; citronellol, 20 to 37 per cent; alcohols such as nerol, farnesol, eugenol, linalool and phenylethyl alcohol or benzyl carbinol, $C_6H_5C_2H_4OH$; esters, aldehydes, citral and a stearopten which is a mixture of paraffin hydrocarbons.

The pure oil is very expensive, since it requires 3000 to 5000 Kg. of fresh petals to yield 1 Kg. of oil; hence the commercial article is grossly adulterated—at place of distillation in Bulgaria—with palmarosa oil (Turkish geranium oil), and in the open market with a host of other substances.

As these adulterants contain no stearopten, the congealing point test of the former Pharmacopœia was aimed to distinguish the pure oil from adulterated specimens, but as the spermaceti is added to sophisticated oils to make up for the lack of the true stearopten, the test loses some of its value. As palmarosa oil consists largely of geraniol, assays for that body have no value in determining purity of rose oil; hence chemists rely chiefly on the saponification number (see p. 1022). While the saponification number of oil of rose is 10 to 17, that of palmarosa oil is 30 to 50.

Oil of rose is used almost exclusively as a perfume. It is an ingredient of *ointment of rose water* (U.S.P. XI).

OLEUM ROSMARINI—Oil of Rosemary

(Ol. Rosmar.—Rosemary Oil)

Oil of Rosemary is the volatile oil distilled with steam from the fresh flowering tops of *Rosmarinus officinalis* Linné (Fam. *Labiatæ*).

Oil of Rosemary yields not less than 2.5 per cent of esters calculated as bornyl acetate ($C_{10}H_{17}.C_2H_3O_2$), and not less than 10 per cent of total borneol ($C_{10}H_{17}OH$), free and as esters.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless or pale yellow liquid; characteristic odor; camphoraceous taste; soluble in 10 volumes of 80 per cent alcohol; sp. gr., 0.894 to 0.912; optical rotation, 0 degree to +10 degrees; refractive index, 1.4640 to 1.4760. For details, see U.S.P., p. 266.

For *assay,* see U.S.P., p. 267.

Composition.—Pinene, camphene, cineol, camphor, borneol, esters, etc.

Remarks.—It will be seen from the official definition that the official oil must contain 2.5 per cent of ester and 10 per cent borneol. The ester estimation is by saponification number, while the borneol is assayed by means of the acetylization test. The latter, like the saponification test, will be explained in chapter on Volumetric Analysis (p. 1023).

Medical Properties.—Carminative.

Dose.—0.1 cc. (1½ minims).

OLEUM SANTALI—Oil of Santal

(Ol. Santal.—Sandalwood Oil)

Oil of Santal is the volatile oil distilled with steam from the dried heartwood of *Santalum album* Linné (Fam. *Santalaceæ*).

Oil of Santal yields not less than 90 per cent of alcohols calculated as santalol ($C_{15}H_{24}O$).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Pale yellow, somewhat viscid, oily liquid; characteristic odor; soluble in 5 volumes of 70 per cent alcohol; sp. gr., 0.965 to 0.980; optical rotation, −15 degrees to −20 degrees in 100-mm. tube; refractive index, 1.5000 to 1.5100. For details, see U.S.P., p. 267.

For *assay*, see U.S.P., p. 267.

Composition.—Santalol (a mixture of two isomeric alcohols, $C_{15}H_{24}O$); santalene (a mixture of two isomeric sesquiterpenes, $C_{15}H_{24}$); ekasantalal, (an aldehyde, $C_{11}H_{16}O$); santanone (a mixture of ketones, including true santanone, $C_{11}H_{16}O$, and nor-camphor, $C_9H_{14}O$); santanone alcohol, $C_9H_{16}O$; a hydrocarbon, $C_{11}H_{18}$; teresantalol, an alcohol, $C_{10}H_{16}O$; teresantalic acid, $C_9H_{13}COOH$, and esters of the above-mentioned alcohols and acids.

Remarks.—It will be noted that this oil comes from a different source than the official red saunders.

Medical Properties.—Antiseptic in gonorrhea.

Dose.—0.5 cc. (8 minims).

Santalol esters are now being marketed as gonorrhea remedies. Thus **Santyl** (N.N.R.) is the neutral salicylic ester of santalol.

Oleum Thymi (N.F. VI), or *Oil of Thyme*, is obtained by distillation from the flowering plant of *Thymus vulgaris.* It is a colorless or red liquid of characteristic odor and taste and contains thymol, cumene, *l*-pinene, borneol, linalool and carvacrol. It is used as a carminative and antiseptic in 1½ minim doses and is a constituent of *antiseptic solution*, N.F. (p. 213).

VALERIANA—Valerian

(Valer.)

Valerian consists of the dried rhizome and roots of *Valeriana officinalis* Linné (Fam. *Valerianaceæ*).

Valerian contains not more than 5 per cent of foreign organic matter and yields not more than 10 per cent of acid-insoluble ash.

Constituents.—Volatile oil, 2 alkaloids (chatamine and valerine), resin, acids, etc.

The volatile oil is composed of the terpenes, camphene and pinene; borneol esters, chiefly the valerianate, 9.5 per cent, and several other bodies. It is now thought that all the valerianic acid present is in the form of the ester above mentioned.

Medical Properties.—Sedative in hysteria. Administered as *tincture*, U.S.P. (p. 252), and the *ammoniated tincture*, N.F. (p. 254). The valerianates, or valerates, especially ammonium valerianate, are popular. *Elixir Ammonium Valerate* is recognized by the National Formulary (p. 228).

Dose.—750 mg. (12 grains).

Viburnum Prunifolium (N.F. VI), or *Black Haw*, is the bark of *Viburnum prunifolium.* It contains valeric acid and bitter, resinous principles, one of the latter being called *viburnin.* If it possesses any medicinal activity, it is due to the valerianic acid it contains, hence it can best be considered along with valerian. Bear in mind, however, that the *drug contains no volatile oil*, hence its study in this chapter is, to a certain extent, inconsistent and possibly misleading. The drug is popularly esteemed as a nervine, especially in internal disorders; having been of late largely advertised among physicians, through the exploiting of a proprietary preparation. The Formulary recognizes the *fluidextract* (p. 271). *Dose*, 2 Gm. (30 grains).

Viburnum Opulus (N.F. VI), or *Cramp Bark*, is properly obtained from *Viburnum opulus*, var. *Americanum* (Miller) Aiton (Fam. *Caprifoliaceæ*), although much of the Viburnum opulus of commerce consists almost entirely of the bark of *Acer spicata.* Its value, if any, like that of black haw, is due to the valerianic acid which it contains. *Dose*, 30 grains.

Sassafras (N.F. VI) is the bark of the root of *Sassafras variifolium.* It contains volatile oil (7 per cent); resin; a tannin-like body, called *sassafrid*, and tannic acid. It is used as a carminative and diaphoretic in 10-Gm. doses.

OLEUM SASSAFRAS—Oil of Sassafras

(Ol. Sassaf.—Sassafras Oil)

Oil of Sassafras is the volatile oil distilled with steam from the root of *Sassafras variifolium* (Salisbury) O. Kuntze (Fam. *Lauraceæ*).

Note.—If the oil has solidified in whole or in part, carefully warm it at a low temperature until it is liquefied, then thoroughly mix it before dispensing.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Yellow or reddish-yellow liquid; characteristic odor and taste; soluble in 2 volumes of 90 per cent alcohol; sp. gr., 1.065 to 1.077; optical rotation, +2 degrees to +4 degrees in 100-mm. tube; refractive index, 1.5200 to 1.5350. For details, see U.S.P., p. 268.

For *tests for identity* and for *impurities* (heavy metals), see U.S.P., p. 268.

Composition.—Safrol, 80 per cent; pinene and phellandrene, 10 per cent; dextrogyrate camphor, 6.8 per cent; eugenol, sesquiterpenes, etc.

Medical Properties.—Stimulant and carminative. Used largely in liniments.

Dose.—0.1 cc. (1½ minims).

CINNAMOMUM—Cinnamon

(Cinnam.—Saigon Cinnamon)

Cinnamon is the dried bark of *Cinnamomum Loureirii* Nees (Fam. *Lauraceæ*).

Cinnamon yields not less than 2 per cent of volatile, ether-soluble extractive and not more than 2 per cent of foreign organic matter.

Storage.—Preserve in well-closed containers.

Constituents.—Volatile oil, mucilage, only traces of starch, etc.

While U.S.P. 1890 recognized three varieties of cinnamon bark: cassia cinnamon from *Cinnamomum cassia,* Ceylon cinnamon from *Cinnamomum zeylonicum,* and Saigon cinnamon from *Cinnamomum Loureirii* and while U.S.P. IX recognized both Ceylon and Saigon cinnamons, the present Pharmacopœia recognizes only the Saigon variety. Cassia and Saigon cinnamon are reddish brown barks of ordinary size while Ceylon cinnamon, which is the inner bark, is as thin as paper, and comes in tightly rolled quills. The oil from these two barks is not identical with the official oil. Cinnamon is used in *compound tincture of cardamom* (U.S.P.), *compound tincture of lavender* (U.S.P.), *aromatic tincture of rhubarb* (U.S.P.) and *compound tincture of gambir* (N.F.).

Medical Properties.—Carminative, flavor.

Dose.—250 milligrams (4 grains).

OLEUM CINNAMOMI—Oil of Cinnamon

(Ol. Cinnam.—Oil of Cassia)

Oil of Cinnamon is the volatile oil distilled with steam from the leaves and twigs of *Cinnamomum Cassia* (Linné) Blume (Fam. *Lauraceæ*), rectified by distillation. Oil of Cinnamon contains not less than 80 per cent by volume of cinnamic aldehyde (C_9H_8O).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Yellowish or brownish liquid, darkens and thickens on aging and on exposure to the air; characteristic odor and taste; soluble in 1 volume of alcohol, U.S.P., and in 2 volumes of 70 per cent alcohol; also soluble in glacial acetic acid; sp. gr., 1.045 to 1.063; optical rotation, +1 degree to −1 degree in 100-mm. tube; refractive index, 1.6020 to 1.6135. For details, see U.S.P., p. 252.

For *tests for identity* and for *impurities* (heavy metals, rosin, chlorinated products), see U.S.P., p. 252.

For *assay,* see U.S.P., p. 253.

Composition.—Cinnamic aldehyde, 75 to 90 per cent; salicyl aldehyde, coumarin, free cinnamic acid, etc.

Remarks.—While U.S.P. IX did not mention which part of the cinnamon plant furnished the oil, U.S.P. XI does specify that it should be distilled from the leaves and twigs of the plant. The oil is not identical with that from Ceylon cinnamon; in fact, the only point of similarity is that the bulk of both oils consists of cinnamic aldehyde. Cinnamic acid present in the oil attacks metals, and as the oil is shipped from China in lead containers, that metal is apt to be found in the oil; hence the pharmacopœial test for heavy metals.

Medical Properties.—Stimulant, carminative, rubefacient, flavor. Used in preparing *cinnamon water*, U.S.P. (p. 199), and *spirit of cinnamon*, U.S.P. (p. 204).

Dose.—0.1 cc. (1½ minims).

Eucalyptus (U.S.P. X) is the dried scythe-shaped leaf of *Eucalyptus Globulus.* It contains 6 per cent of volatile oil, chlorophyll, resin, tannin, etc. It is used as a stimulant, carminative and antiseptic in 30 grain doses.

OLEUM EUCALYPTI—Oil of Eucalyptus

(Ol. Eucalypt.—Eucalyptus Oil)

Oil of Eucalyptus is the volatile oil distilled with steam from the fresh leaves of *Eucalyptus globulus* Labillardière, or from other species of *Eucalyptus* (Fam. *Myrtaceæ*). Oil of Eucalyptus contains not less than 70 per cent of eucalyptol ($C_{10}H_{18}O$).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless or pale-yellow liquid; characteristic camphoraceous odor; pungent, spicy, cooling taste; soluble in 5 parts of 70 per cent alcohol; sp. gr., 0.905 to 0.925; optical rotation, −10 degrees to +10 degrees; refractive index, 1.4580 to 1.4700. For details, see U.S.P., p. 254.

For *tests for identity* and for *impurities* (other eucalyptus oils containing much phellandrene, heavy metals), see U.S.P., p. 254.

For *assay* (congealing point), see U.S.P. and also below.

Composition.—Eucalyptol (or cineol), 50 per cent; dextrogyrate pinene; other terpenes (little or no phellandrene), etc.

Some eucalyptus oils contain *cryptal* or isopropyl-cyclohexene aldehyde, a derivative of α-phellandrene.

Remarks.—While U.S.P. IX directed that this oil be assayed by precipitation of the cineol as arsenate and then separating the cineol and measuring it as such, the present Pharmacopœia determines the quality of the oil through its congealing point. Note that eucalyptol (or cineol) is official (p. 833).

Medical Properties.—Antiseptic.

Dose.—0.5 cc. (8 minims).

Buchu (U.S.P. X; N.F. VI) is the dried leaf of *Barosma betulina* and other species of *Barosma.* The two commercial forms are long and short buchu. It contains volatile oil, fat, mucilage, chlorophyll, etc.

The *volatile oil* contains a stearopten, *diosphenol* and a glucoside, *diosmin.* The eleoptene consists of a terpene, $C_{10}H_{18}$, and a ketone resembling menthone. The most prominent characteristic of this valuable drug of South Africa is its peculiar and pleasant odor. It is used as a stimulant and diuretic. Administered as infusion and as *fluidextract* and as *compound fluidextract* (N.F. VI) (p. 270). A number of *elixirs* of buchu are recognized by the Formulary. *Dose*, 2 Gm. (30 grains).

Hedeoma (U.S.P. VIII), or *Pennyroyal*, is the dried leaves and flowering tops of *Hedeoma pulegioides* (Linné) Persoon (Fam. *Labiatæ*). Its chief constituent is its volatile oil. It is used as a diaphoretic, emmenagogue, carminative, in 120-grain doses.

Oleum Hedeomæ (U.S.P. VIII), or *Oil of Pennyroyal*, is distilled from the leaves and flowering tops of Hedeoma. It contains pulegone, $C_{10}H_{16}O$ (24 per cent), methylcyclohexanone (6 per cent), menthone (50 per cent), pinene, limonene, dipentene, a sesquiterpene alcohol, a phenol, formic, butyric and other acids, free and combined. It is an emmenagogue and as it is frequently used as an abortifacient, its sale is prohibited in many States. *Dose*, 3 minims.

MENTHA PIPERITA—Peppermint
(Menth. Pip.)

Peppermint consists of the dried leaves and tops of *Mentha piperita* Linné (Fam. *Labiatæ*).

Peppermint contains not more than 2 per cent of stems over 3 mm. in diameter, or other foreign organic matter.

Constituents.—Volatile oil, tannic acid, etc.

Medical Properties.—Carminative, stimulant, flavor. The herb is used to color the official *spirit of peppermint* (p. 204).

Dose.—4 Gm. (60 grains).

OLEUM MENTHÆ PIPERITÆ—Oil of Peppermint
(Ol. Menth. Pip.—Peppermint Oil)

Oil of Peppermint is the volatile oil distilled with steam from the fresh, overground parts of the flowering plant of *Mentha piperita* Linné (Fam. *Labiatæ*), rectified by steam distillation.

Oil of Peppermint yields not less than 5 per cent of esters, calculated as menthyl acetate ($C_{10}H_{19}.C_2H_3O_2$), and not less than 50 per cent of total menthol ($C_{10}H_{19}.OH$), free and as esters.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless liquid; strong odor of peppermint; pungent taste, followed by sensation of cold when air is drawn into the mouth; sp. gr., 0.896 to 0.908; optical rotation, −18 degrees to −32 degrees in 100-mm. tube; refractive index, 1.4600 to 1.4710. For details, see U.S.P., p. 259.

For *tests for identity* and for *impurities* (dementholized oil, dimethyl sulfide, oil of *M. arvensis*), and for *assay*, see U.S.P., p. 259.

Composition.—Menthol, U.S.P.; menthyl acetate; menthene and fourteen other bodies.

Remarks.—The different peppermint oils—American, English, Japanese, German—are not identical in chemical composition, the statement just given referring to the American oil. Thus the Japanese oil contains 70–91 per cent total menthol, the English 58 to 66 per cent, while the American has 50 to 60 per cent. The menthol content was formerly considered the criterion of quality of the oil; hence the test provided in the former Pharmacopœias that a sample of oil placed in freezing mixture should yield crystals of menthol. Experience has shown, however, that some of the oils of the best quality did not respond to this test, which was, therefore, omitted in the tenth revision.

Medical Properties.—Carminative and flavor. Administered as *spirit*, U.S.P. (p. 204). The oil is a constituent of *peppermint water*, U.S.P. (p. 200).

Dose.—0.1 cc. (1½ minims).

MENTHA VIRIDIS—Spearmint
(Menth. Vir.)

Spearmint consists of the dried leaves and tops of *Mentha spicata* Linné (Fam. *Labiatæ*).

Spearmint contains not more than 2 per cent of stems over 3 mm. in diameter, or other foreign organic matter.

Constituents.—Volatile oil, resin, etc.

Medical Properties.—Similar to peppermint.

OLEUM MENTHÆ VIRIDIS—Oil of Spearmint
(Ol. Menth. Vir.—Spearmint Oil)

Oil of Spearmint is the volatile oil distilled with steam from the fresh, overground parts of the flowering plant of *Mentha spicata* Linné (*Mentha viridis* Linné) (Fam. *Labiatæ*).

Oil of Spearmint yields not less than 50 per cent, by volume, of carvone ($C_{10}H_{14}O$).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless, yellow or greenish-yellow liquid; characteristic odor and taste; soluble in 1 volume of 80 per cent alcohol; sp. gr., 0.917 to 0.934; optical rotation, −48 degrees to −59 degrees in 100-mm. tube; refractive index, 1.4820 to 1.4900. For details, see U.S.P., p. 260.

Assay.—Like oil of caraway.

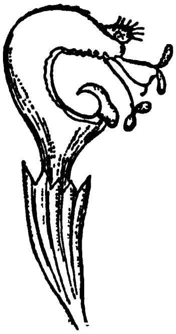


Fig. 270.—Horsemint flower.

Composition.—Levogyre carvone, 50 per cent; limonene, phellandrene, dihydrocarvenone.

Medical Properties.—Like oil of peppermint. The *spirit* (p. 205) is made from the oil and a small amount of the herb and the *water* (p. 200) is made from the oil and an absorbent powder.

Dose.—0.1 cc. (1½ minims).

Peppermint and spearmint are representatives of the *Labiatæ*, the "lip family," or mint family; this group of plants being so called because the flowers of this family have their petals united with a two-lipped corolla, as shown in (Fig. 270), the flower of the horsemint.

The plants of this family are characterized by the presence of aromatic volatile oils, and a large number of them are used in medicine. Among those formerly official may be cited *pennyroyal, scullcap, boneset, melissa* (Balm), *catnip, thyme,* and *origanum.*

CARYOPHYLLUS—Clove
(Caryoph.—Cloves)

Clove is the dried flower buds of *Caryophyllus aromaticus* Linné (Fam. *Myrtaceæ*).

Clove contains not more than 5 per cent of its stems and not more than 1 per cent of other foreign organic matter, and yields not less than 15 per cent of volatile ether-soluble extractive, not more than 10 per cent of crude fiber, and not more than 0.75 per cent of acid-insoluble ash.

Constituents.—Volatile oil, *caryophyllin,* tannin, gum resin, fixed oil.

Caryophyllin occurs as silky needles melting at 310° C. It is isomeric with ursone, both having the formula, $C_{30}H_{48}O_3$. Dodge inclines to the opinion that caryophyllin is a derivative of cholesterol (see p. 747).

Remarks.—Cloves are not fruit or seed, as is commonly believed, but are flower buds. Sliced lengthwise, the sample is found hollow in the upper parts, where will be found the stamens, which look like dried threads. Cloves are used as a spice, and are largely adulterated. For instance, whole cloves from which the oil has been distilled have been put on the market. These are detected by the fact that such exhausted cloves float horizontally on the surface of water, while the true article, containing the heavy volatile oil, will either sink or float in an upright position. The powder is adulterated with starchy material or with mineral substances, which impurities can be detected by the fact that pure powdered cloves, when viewed under the microscope, contain few or no starch grains, and yield, on burning, no more than 0.75 per cent of acid-insoluble ash.

Clove is used in the following official preparations: *compound tincture of lavender* and *aromatic tincture of rhubarb*.

Dose.—250 mg. (4 grains).

OLEUM CARYOPHYLLI—Oil of Clove

(Ol. Caryoph.—Oil of Cloves)

Oil of Clove is the volatile oil distilled with steam from the dried flower buds of *Caryophyllus aromaticus* Linné (Fam. *Myrtaceæ*). Oil of Clove contains not less than 82 per cent by volume of eugenol ($C_{10}H_{12}O_2$).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless or pale yellow liquid, darkens and thickens on age and on exposure to the air; characteristic odor and taste; soluble in 2 volumes of 70 per cent alcohol; sp. gr., 1.038 to 1.060; optical rotation, not more than −1 degree, 30 minutes, in 100-mm. tube; refractive index, 1.5300 to 1.5350. For details, see U.S.P., p. 250.

For *tests for identity* and for *impurities* (phenol, heavy metals), see U.S.P., p. 250.

Outline of Assay.—The oil is shaken with potassium hydroxide solution in a cassia flask; the flask is filled to the graduations with the alkaline solution and the volume of the insoluble portion is read. For details, see U.S.P., p. 250.

Composition.—Eugenol (80 to 92 per cent); a number of alcohols (methyl, methylamyl, furfuryl, benzyl, etc.); a number of ketones (acetone, methylamyl ketone, etc.); several aldehydes (dimethylfuryl aldehyde, etc.); esters (methyl salicylate, etc.); and caryophyllene.

Remarks.—The assay given above is based upon the principle that the phenol, eugenol, dissolves in alkaline solution, leaving the terpenes undissolved. The volume of the insoluble terpenes is read and from the figure the volume of the soluble eugenol may be deduced.

Medical Properties.—Stimulant. Used in toothache.

Dose.—0.1 cc. (1½ minims).

Anisum (N.F. VI), or *Aniseed*, represents the fruit of *Pimpinella anisum*. It contains volatile oil, fixed oil, carbohydrates and proteins. Its appearance closely resembles the poisonous conium fruit (p. 940). Anise is used as a carminative, stimulant and flavor. *Dose*, 500 mg. (8 grains).

Illicium, or *Star Anise*, the fruit of *Illicium verum*, was official in the Pharmacopœia of 1890, and is here mentioned because it yields an oil identical with that from anise.

OLEUM ANISI—Oil of Anise

(Ol. Anisi—Anise Oil)

Oil of Anise is the volatile oil distilled with steam from the dried ripe fruit of *Pimpinella anisum* Linné (Fam. *Umbelliferæ*) or from the dried ripe fruit of *Illicium verum* Hooker filius (Fam. *Magnoliaceæ*).

Note.—If solid material has separated, carefully warm the mixture at a low temperature until it is completely liquefied, and mix it thoroughly before using.

Storage.—Preserve in well-filled bottles, in a cool place and protected from light.

Summarized Description.

Colorless or pale yellow, strongly refractive liquid; characteristic odor and taste; soluble in 3 volumes of 90 per cent alcohol; sp. gr., 0.978 to 0.988; optical rotation, +1 degree to −2 degrees in 100-mm. tube; refractive index, 1.5530 to 1.5600. For details, see U.S.P., p. 249.

For *tests for identity* and for *impurities* (phenols, heavy metals), see U.S.P., p. 249.

For *congealing point* (not less than 15° C.), see U.S.P., p. 249.

Constituents.—Anethol, 80 to 90 per cent; methyl chavicol. Both have formula, $C_{10}H_{12}O$.

Duncan and other investigators found that star anise oil contains 0.2 per cent of terpenes (pinene, phellandrene, limonene, dipentene, etc.) and 0.28 per cent of sesquiterpenes. Mareeuw differentiates between oil of anise and oil of star anise, by use of a color test.

Remarks.—As anethol is a solid, the congealing point of the oil (15° C.) is a criterion of value.

Medical Properties.—Carminative and flavor. Used in making *anise water* (p. 198) and *spirit of anise* (p. 203). It is also a constituent of *paregoric* (p. 251) and of *compound spirit of orange* (p. 203).

Dose.—0.1 cc. (1½ minims).

Coriandrum (N.F. VI), or *Coriander Seed*, represents the fruit of *Coriandrum sativum*. It contains volatile oil (¼ to ½ per cent); fixed oil, etc. It is used as a carminative and aromatic in 30-grain doses.

OLEUM CORIANDRI—Oil of Coriander

(Ol. Coriand.—Coriander Oil)

Oil of Coriander is the volatile oil distilled with steam from the dried ripe fruit of *Coriandrum sativum* Linné (Fam. *Umbelliferæ*).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless or pale yellow liquid, characteristic odor and taste; soluble in 3 volumes of 70 per cent alcohol; sp. gr., 0.863 to 0.875; optical rotation, +8 degrees to +15 degrees in 100-mm. tube; refractive index, 1.4620 to 1.4720. For details, see U.S.P., p. 253.

For *tests for identity* and for *impurities* (heavy metals), see U.S.P., p. 253.

Composition.—Pinene, cymene and other terpenes: d-linalool, geraniol, l-borneol, and their acetic esters; decylic alcohol.

Medical Properties.—Carminative. A constituent of *syrup of senna* (p. 221) and of *compound spirit of orange* (p. 203).

Dose.—0.1 cc. (1½ minims).

Fœniculum (N.F. VI), or *Fennel Seed*, represents the fruit of *Fœniculum vulgare*. Fennel contains volatile oil (2 to 4 per cent); fixed oil, etc. It is used as a carminative and stimulant and is a constituent of a *compound infusion of senna*, N.F. (p. 238). *Dose*, 1 Gm. (15 grains).

OLEUM FŒNICULI—Oil of Fennel

(Ol. Fœnic.—Fennel Oil)

Oil of Fennel is the volatile oil distilled with steam from the dried ripe fruit of *Fœniculum vulgare* Miller (Fam. *Umbelliferæ*).

Note.—*If solid material has separated, carefully warm the oil at a low temperature until it is completely liquefied and thoroughly mix it before using.*

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless or pale yellow liquid; characteristic odor and taste; soluble in 8 volumes of 80 per cent alcohol and 1 volume of 90 per cent alcohol; sp. gr., 0.953 to 0.973; optical rotation, +12 degree to +24 degree in 100-mm. tube; refractive index, 1.5280 to 1.5380. For details, see U.S.P., p. 254.

For *tests for identity*, for *impurities* (heavy metals) and for *congealing point* (at least 3° C.), see U.S.P., p. 254.

Composition.—*Anethol*, 50 to 60 per cent; *fenchone*, a ketone having formula $C_{10}H_{16}O$; parapropenyl phenol, $C_{14}H_{18}O$; pinene; dipentene; etc.

Medical Properties.—Carminative. Very popular among German physicians as a constituent of digestive powders. It is a constituent of *compound licorice powder* (p. 316) and of *fennel water* (p. 200).

Dose.—0.1 cc. (1½ minims).

CARUM—Caraway

(Caraway Fruit, Caraway Seed)

Caraway is the dried ripe fruit of *Carum Carvi* Linné (Fam. *Umbelliferæ*).

Caraway contains not more than 3 per cent of other fruits, seeds or foreign organic matter, and yields not more than 1.5 per cent of acid-insoluble ash.

Constituents.—Volatile oil, 5 per cent; fixed oil, resin.
Medical Properties.—Carminative, stimulant, flavor.
Dose.—1 Gm. (15 grains).

Oleum Cari (U.S.P. X; N.F. VI), or *Oil of Caraway*, is the volatile oil distilled from the fruit of *Carum Carvi.* It contains 50 to 60 per cent of carvone, dextrogyrate limonene, etc. It is used as a carminative in 1½-minim doses.

Petroselinum (U.S.P. IX), or *Parsley Seed*, represents the fruit of *Petroselinum sativum.* It contains volatile oil (1.4 per cent); fixed oil (22 per cent); pectin; chlorophyll; tannin; *apiol* (p. 820). It is used as an emmenagogue usually in the form of the oleoresin (p. 276).

The drugs last studied—anise, fennel, coriander, caraway and parsley—are representatives of the Umbelliferæ; the parsley family, whose flowers are arranged on stalks which radiate like rods of an umbrella, as shown in Fig. 271.

Most official drugs yielded by the Umbelliferæ are fruit, which are, unfortunately, commonly called "seeds."

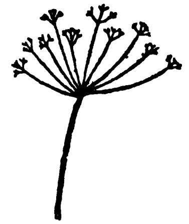


Fig. 271.—Inflorescence of umbellifera (schematic).

A fruit can vary from a seed, with its dry ovary wall, to very elaborate fruit, which include several other organs attached to the ovary. Thus, when we examine an apple, we find three distinct layers—the red skin, the white meat, and the papery core surrounding the seed. Of these layers, only the core represents the ovary wall, the meat and skin being a modification of another part of the flower—the green calyx. On the other hand, an acorn likewise represents a true fruit, the cup being a cluster of leaves at the base of the ripened ovary, the latter being the "nut." From this can be separated the outer coat, which represents the ovary wall, while the "kernel" within, with its shaggy coat, represents the seed. Similarly, the so-called "seeds"—*anise, caraway, coriander,* and *fennel*—are fruit just as are apples and acorns, and, like the acorn, the ovary wall is inconsiderable, and does not separate from the seed of its own free will.

Pimenta (N.F. V), or *Allspice*, is the dried, nearly ripe fruit of *Pimenta officinalis* Lindley (Fam. *Myrtaceæ*). It contains volatile oil, resin, fixed oil, chlorophyll and traces of alkaloid. It is used as a stomachic and carminative in 15-grain doses.

Oleum Pimentæ (N.F. VI), or *Oil of Allspice*, is a colorless, yellow or reddish liquid of a characteristic odor and taste. It contains eugenol, sesquiterpenes, etc. and is used as a carminative and flavor. It is an ingredient of *compound spirit of myrcia*, N.F.

CARDAMOMI SEMEN—Cardamom Seed
(Cardam. Sem.)

Cardamom Seed is the dried ripe seed of *Elettaria cardamomum* Maton (Fam. *Zingiberaceæ*), recently removed from the capsules.

Cardamom Seed yields not more than 5 per cent of acid-insoluble ash.

Constituents.—Volatile oil, fixed oil, starch, etc. The volatile oil consists of terpenes (dipentene and terpene), borneol, terpineol, cineol, sabinene, terpinyl acetate.

Remarks.—While former Pharmacopœias recognized the entire fruit of cardamom, including the pericarp (or "hulls" or "capsules") the present Pharmacopœia directs the use of seed only. Like all drugs used as spices, the commercial powder is apt to be adulterated with mineral matter, hence the Pharmacopœia directs that it should yield not more than 5 per cent of ash.

Medical Properties.—Carminative, stomachic. Official preparation: the *compound tincture* (p. 246). Also used in *compound tincture of gentian* (p. 248), and in *compound tincture of rhubarb* (p. 254) and *sweet tincture of rhubarb* (p. 256).

Dose.—1 Gm. (15 grains).

Oleum Cardamomi (N.F. VI) is the volatile oil obtained from cardamom seed. It is an ingredient of *compound spirit of cardamom* (p. 206) and *compound spirit of vanillin* (p. 206).

Sabal (N.F. VI), or *Saw Palmetto Berries*, is the fruit of *Serenoa serrulata*. It contains fixed oil (ethyl ethers of caproic, caprylic, oleic, and other acids), about 1.6 per cent; sugar (pentoses), 5.4 per cent. The presence of an alkaloid is a subject of dispute.

The so-called "volatile oil" is merely an ethyl ester of the various fatty acids found in the fruit. It is noted only in alcoholic galenicals of the drug. There has been considerable controversy as to the therapeutic value of this drug; some manufacturers claiming that only the fresh fruit should be used in making preparations of the drug.

Saw palmetto is supposedly a tonic and stimulant, especially to the reproductive organs; this opinion being largely due to the advertising of nostrum makers. *Dose*, 1 Gm. (15 grains).

AURANTII AMARI CORTEX—Bitter Orange Peel

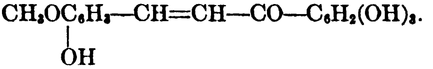
(Aurant. Amar. Cort.)

Bitter Orange Peel is the dried rind of the unripe fruit of *Citrus Aurantium* Linné (Fam. *Rutaceæ*).

Constituents.—Volatile oil; *hesperidin;* an acid, $C_{44}H_{28}O_{14}$; resin; *aurantiamarin*, a bitter glucoside.

The volatile oil is chemically identical with that of sweet orange, except that it has a bitter taste, due to the aurantiamarin it contains. This oil is not official.

Hesperidin is a glucoside, hydrolyzing to rhamnose, glucose and *hesperetin*. (See p. 714). The latter is a phenol resembling eriodictyol and supposedly having the formula



$$\underset{\displaystyle OH}{CH_3OC_6H_3}—CH=CH—CO—C_6H_2(OH)_3.$$

Medical Properties.—Aromatic bitter. Official preparations, the *tincture* (p. 244) *compound tincture of cinchona* (p. 246), and *compound tincture of gentian* (p. 248).

Dose.—1 Gm. (15 grains).

AURANTII DULCIS CORTEX—Sweet Orange Peel

(Aurant. Dulc. Cort.)

Sweet Orange Peel is the fresh, outer rind of the nonartificially colored, ripe fruit of *Citrus Aurantium* var. *sinensis* Linné (Fam. *Rutaceæ*).

Constituents.—Volatile oil; *hesperidin*, $C_{22}H_{26}O_{12}$, a glucoside that hydrolyzes to *hesperetin*, $C_{16}H_{14}O_6$; a phytosterolin identical with ipuranol (p. 714); 2 phytosterols. The yellow color of the peel is due to an ether-soluble carotinoid (p. 882).

Remarks.—Note that the Pharmacopœia directs the use of the outer rind—that is, the thin yellow layer must be separated from the thick white layer (the *zest*). This is important in making pharmaceuticals, since the zest contains a body that blackens with iron salts, and the same will be true of preparations made from the peel not freed from the zest. It is used in *tincture of sweet orange* (p. 244).

OLEUM AURANTII—Oil of Orange

(Ol. Aurant.—Orange Oil, Oil of Sweet Orange)

Oil of Orange is the volatile oil obtained by expression from the fresh peel of the ripe fruit of *Citrus Aurantium* var. *sinensis* Linné (Fam. *Rutaceæ*).

Note.—Oil of Orange which has a terebinthinate odor must not be used or dispensed.

Storage.—Preserve in well-filled bottles, in a cool place and protected from light.

Summarized Description.

Yellow liquid; characteristic odor and taste; sp. gr., 0.842 to 0.846; refractive index, 1.4723 to 1.4737; optical rotation, +94 degrees to +99 degrees in 100-mm. tube; first 5 cc. of distillate from 50 cc. of oil should have almost the same refraction and rotation as the original oil. For details, see U.S.P., p. 249.

For *tests for identity* and for *impurities* (washed citrus oils, heavy metals), see U.S.P., p. 249.

Composition.—Dextrogyrate limonene, 90 per cent; *citral*, derivative of anhydrogeraniol (p. 824); citronellal; methyl anthranilate esters, etc.

Remarks.—As already mentioned (p. 826), the reason why oil of orange and of lemon become terebinthinate is through the conversion of their limonene into dipentene. This change, of course, ruins the quality of the oil, and it is poor pharmacy to use such oils in preparations. Of the several schemes suggested to prevent this decomposition, the best is the adding of a small amount of glycerin—say, half an ounce to 4 ounces of oil—and keeping bottle inverted. In this way the mouth of the bottle is "sealed" with a layer of the glycerin, which prevents access of air. When the oil is to be used, the bottle is placed in an upright position for a few minutes, and the oil decanted from the heavier glycerin layer. This, in the writer's experience, proved more satisfactory than diluting the oil with alcohol. Cottonseed oil or olive oil may be substituted for glycerin in this method. The commercial oil is likely to be adulterated with oil of turpentine or with the terpenes obtained from oil of lemon, after preparation of terpeneless oil (p. 827). The polariscopic and refraction readings of the first distillation fraction of the oil outline above will detect these sophistications.

Medical Properties.—Flavor. It is a constituent of *compound spirit of orange* (p. 203).

Dose.—0.1 cc. (1½ minims).

LIMONIS CORTEX—Lemon Peel

(Limon. Cort.)

Lemon Peel is the outer yellow rind of the fresh ripe fruit of *Citrus medica* var. *Limon* Linné (Fam. *Rutaceæ*).

Constituents.—Volatile oil; hesperidin; vitamins; etc.

Remarks.—It will be noted that this drug, like orange peel, is the "outer rind" separated from the zest (p. 852).

Medical Properties.—Flavor. Official preparation, *tincture of lemon peel*, p. 249.

OLEUM LIMONIS—Oil of Lemon

(Ol. Limon.—Lemon Oil)

The volatile oil obtained by expression, without the aid of heat, from the fresh peel of the fruit of *Citrus medica* var. *Limon* Linné (Fam. *Rutaceæ*), with or without the previous separation of the pulp and the peel.

Note.—Oil of Lemon which has a terebinthinate odor must not be used or dispensed.

Storage.—Preserve in completely filled, well-stoppered, amber-colored bottles, in a cool place and protected from light.

Summarized Description.

Pale yellow or greenish-yellow liquid, characteristic odor and taste; soluble in 3 volumes of alcohol U.S.P.; sp. gr., 0.851 to 0.855; refractive index, 1.4744 to 1.4755; optical rotation, +57 degrees to +64 degrees in 100-mm. tube; first part of distillate (see oil of orange) should have almost same refraction and rotation as the original oil. For details, see U.S.P., p. 257.

Composition.—Dextrogyrate limonene, 90 per cent; phellandrene; α-pinene; l-camphene, terpinene; sesquiterpenes; citral, 7 to 10 per cent; a crystalline compound, $C_{10}H_{18}O_2$; citronellal; esters, etc.

Medical Properties.—Flavoring. Used in *aromatic spirit of ammonia,* U.S.P. (p. 506) and *compound spirit of orange,* U.S.P. (p. 203). *Spirit of lemon,* U.S.P. 1890, has been replaced by tincture of lemon peel.

Dose.—Of the oil, 0.1 cc. (1½ minims).

Oil of Bergamot (N.F. VI), is obtained by expression of the rind of the bergamot orange, the fruit of *Citrus Aurantium,* var. *Bergamia.* Its green color is due to the presence of copper from its container. It is used as a perfume.

Oil of Neroli, U.S.P. 1890, is the oil obtained by distillation of orange flowers, and is a by-product in the manufacture of orange flower water. It is used in perfumery.

It will be noted that the three oils—orange, lemon, and bergamot—are obtained by expression (as already described on p. 840) of the rind of closely allied fruits; that this group of fruit—orange, lemon, lime, etc.—forms a subdivision of the plant family, *Rutaceæ.*

MYRISTICA—Myristica

(Myrist.—Nutmeg)

Myristica is the dried ripe seed of *Myristica fragrans* Houttuyn (Fam. *Myristicaceæ*), deprived of its seed-coat and arillode and with or without a thin coating of lime.

Myristica yields not less than 25 per cent of nonvolatile, ether-soluble extractive, and not more than 0.5 per cent of acid-insoluble ash.

Constituents.—Volatile oil, about 7 per cent; fat, about 25 per cent; starch, etc. The fat, called *nutmeg butter,* or *oil of mace,* and obtained by expressing nutmeg between hot plates, contains from 2.4 to 12.5 per cent of the essential oil; 42.5 to 73 per cent of the trimyristicin (glyceryl myristate), 5 per cent of tripalmitin, 8.5 per cent of triolein and smaller amounts of free fatty acid.

Medical Properties.—Stimulant, stomachic, flavor. Used in *compound tincture of lavender* (p. 249) and *aromatic tincture of rhubarb* (p. 251).

Dose.—500 mg. (8 grains).

OLEUM MYRISTICÆ—Oil of Myristica

(Ol. Myrist.—Myristica Oil, Oil of Nutmeg)

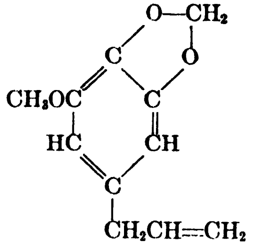
Oil of Myristica is the volatile oil distilled with steam from the dried kernels of the ripe seed of *Myristica fragrans* Houttuyn (Fam. *Myristicaceæ*).

Storage.—Preserve in well-closed, amber-colored bottles, in a cool place and protected from light.

Summarized Description.

Colorless or pale yellow liquid; characteristic odor and taste; soluble in 1 volume of alcohol U.S.P. and in 3 volumes of 90 per cent alcohol; sp. gr., 0.859 to 0.924; optical rotation, +10 degrees to +30 degrees in 100-mm. tube; refractive index, 1.4740 to 1.4880; on evaporation not more than 2 per cent of residue is left. For details, see U.S.P., p. 263.

Constituents.—Eugenol; terpenes (pinene, camphene, dipentene, etc.); alcohols (linalool, borneol, terpineol, etc.); *myristicin;* acids (myristic, formic, acetic, etc.). Myristicin is allyl-methoxy-methylene-dihydroxybenzene:



and is the narcotic constituent of nutmeg.

Medical Properties.—Flavor. A constituent of *aromatic spirit of ammonia* (p. 506).

Dose.—0.03 cc. (½ minim).

Macis (U.S.P. 1890; N.F. IV), or *Mace*, is the arilloid or outer coating of nutmeg seed. It yields a volatile oil, practically identical with that of the nutmeg. The solid "mace oil" contains myristic, macilenic and macilolic acid; a carotin-free xanthophyll, a phytosterol and an amylodextrin. Mace, like nutmeg, is used as a spice.

DRUGS CONTAINING VOLATILE OIL AND RESIN

This class of drugs differs from the volatile oil drugs just considered by the prominence of their resin content. It will be noted that most of the volatile oil drugs just considered contained resinous matter, but these resins were either insignificant as to amount or indifferent as to activity. On the other hand, the drugs now to be considered owe their activity as much to the resin they contain as to their volatile oil, and it will be noted that all the drugs furnishing official pharmaceutic oleoresins (p. 275) are here considered. As to the chemistry of the resinous ingredients of this class of drugs, let it be said that a general consideration of that, little understood class of bodies—the resins—is reserved for a special chapter (Chapter XLVIII), which, perhaps, would be the better place to consider drugs of the class under consideration. However, since these drugs are most prominently characterized by their odor, and this is largely due to the volatile oil they contain, it is well to consider them among the volatile oil drugs. It might be stated that all these resinous drugs should be extracted with stronger alcohol.

Stillingia (N.F. VI), or *Queens Root*, is the root of *Stillingia sylvatica.* It contains volatile oil; resin; *stillingine*, an alkaloid, fixed oil; etc.

One of the resins is the combination of phytosterol with fatty acids (acetic, butyric, valeric, angelic, oleic, etc.). From the other resin was isolated a phytosterolin, $C_{33}H_{56}O_6$, vanillin, umbelliferon, vanillic and other acids. It is a nauseant, and emetic, in small doses and is more or less laxative. The *fluidextract* is recognized by the National Formulary. *Dose*, 2 Gm. (30 grains).

Sumbul (N.F. VI), or *Musk Root*, represents the rhizome and roots of *Ferula Sumbul.* It contains two balsamic resins; volatile oil (about 1 per cent) a glucoside, *umbelliferon*, etc. It is used as a nerve stimulant in 2-Gm. doses. *The extract* is recognized by the National Formulary.

ASPIDIUM—Aspidium

(Male Fern)

Aspidium consists of the rhizome and stipes of *Dryopteris Filix-mas* (Linné) Schott (Fam. *Polypodiaceæ*).

Aspidium yields not less than 1.5 per cent of crude filicin, and not more than 3 per cent of acid-insoluble ash. ***Only such portions as have retained their internal green color may be used.***

Constituents.—Volatile oil; fixed oil; resin; *filicic acid* which is dibutyryl-phloroglucin; *tannaspidic acid; pteritannic acid, felix red,* etc. The volatile oil consists of the hexyl and octyl esters of the fatty acids (butyric, etc.), also free fatty acids.

Remarks.—Characteristic for good quality of this drug is its green color, which fades as the drug becomes old and worthless, hence the pharmacist should use only such samples as are still green.

Medical Properties.—Tapeworm expeller. Used almost entirely in the form of the *oleoresin,* U.S.P. (p. 276).

Miyasaki's experiments do not confirm the generally accepted view of the danger of administering castor oil after the ingestion of male fern preparations.

Dose.—No dose of drug is given in U.S.P. XI. U.S.P. IX directed 4 Gm. (60 grains).

ZINGIBER—Ginger

(Zingib.)

Ginger is the dried rhizome of *Zingiber officinale* Roscoe (Fam. *Zingiberaceæ*) with outer cortical layers removed, known in commerce as Jamaica Ginger.

Ginger contains not less than 4.5 per cent of ether-soluble extractive.

Constituents.—Volatile oil; resin, etc.

The volatile oil contains sesquiterpenes, terpenes, citral, methyl-heptanone, nonylaldehyde, linalool, d-borneol, acetic and caprylic acid esters, chavicol, cineol and a characteristic alcohol *zingiberol,* $C_{15}H_{25}OH$. The resin consists of three distinct resins, and when fused with sodium hydroxide, yields protocatechuic acid. The pungent principle is supposed to be a substance called *gingerol* by Thrush. Nomura has separated this into two bodies, *zingerone,* $C_{11}H_{14}O_3$, and *shogaol,* $C_{17}H_{24}O_3$.

Remarks.—A popular variety of ginger comes from Jamaica, and occurs in handsome lobed pieces coated white with lime. Preserved ginger is the same root collected in the spring when green and succulent and boiled with syrup.

Medical Properties.—Carminative, stimulant, flavor. Official preparation: *fluidextract* (p. 266). The last is used in making the *syrup* (N.F. VI). Powdered ginger is a constituent of *compound powder of rhubarb* (N.F. VI) (p. 316).

Dose.—Of drug, 600 mg. (10 grains).

Calamus (N.F. VI), or *Sweet Flag,* is the peeled, dried rhizome of *Acorus Calamus* Linné (Fam. *Araceæ*). It contains volatile oil, resin, *acorin, calamine* and starch.

The *volatile oil* consists of pinene, a sesquiterpene, fatty acids (acetic, heptylic, palmitic, etc.), eugenol, asarone and asaryl aldehyde, and calamus camphor, or calameone, $C_{15}H_{26}O_2$, which has a structure resembling cineol.

Acorin is a bitter glucoside that hydrolyzes to glucose and a terpene and which oxidizes to *acoretin.*

Calamus is used as a carminative, stimulant, and flavor. The whole peeled root is used for teething infants to chew upon. *Dose,* 45 grains.

Orris Root consists of the dried rhizomes of three different cultivated species of *Iris.* It is grown extensively on the hillsides around the Italian city of Florence. The dried rhizome contains two principles, *iridin* and *irigenin.* Upon distillation or upon extraction with a suitable solvent, orris yields about 3 per cent of an odorous concrete, *iris butter,* containing six aliphatic acids (from "C_9" to "C_{13}") and also benzoic acid. It also contains 5 to 10 per cent of *irone,* $C_{13}H_{20}O_1$, a ketone, $C_{10}H_{18}O$, and myristic acid. Orris is used largely as a perfuming agent.

Leptandra (N.F. VI), or *Culver's Root,* is the dry rhizome and roots of *Veronica virginica.* It contains cinnamic and methoxycinnamic acids, sugar, mannitol, tannic acid, coloring matter, a phytosterol and a bitter amorphous product. Glucosides and saponins are not present. The drug was used as a drastic cathartic and the National Formulary recognizes the *fluidextract* (p. 271) and the *extract* (p. 304). *Dose*, 15 grains.

Cimicifuga (U.S.P. X; N.F. VI), or *Black Cohosh, Black Snake root*, or *Macrotys*, consists of the dried rhizome and roots of *Cimicifuga racemosa*. It contains acids (oleic, palmitic, isoferulaic, etc.); sugar; tannin; phytosterols, trace of alkaloid, etc. It is used as a tonic and "blood purifier" in domestic practice and is the constituent of a number of "patent" medicines. *Dose*, 1 Gm. (15 grains).

SERPENTARIA—Serpentaria

(Serpent.)

Serpentaria consists of the dried rhizome and roots of *Aristolochia Serpentaria* Linné, known in commerce as Virginia Snakeroot, or of *Aristolochia reticulata* Nuttall, known in commerce as Texas Snakeroot (Fam. *Aristolochiaceæ*).

Serpentaria contains not more than 10 per cent of its overground stems and not more than 2 per cent of other foreign organic matter, and yields not more than 10 per cent of acid-insoluble ash.

Constituents.—Volatile oil; bitter principle, similar to quassin; resin, *aristolochine.*

The volatile oil consists chiefly of borneol; the Texas snakeroot containing also pinene.

Remarks.—It will be observed that official serpentaria is derived from two different plants, the drugs, however, being practically identical in medicinal action.

Medical Properties.—Popular tonic and "blood purifier." The drug is a constituent of *compound tincture of cinchona* (p. 246).

Dose.—1 Gm. (15 grains).

Ginseng, the roots of *Panax quinquefolium*, enjoys enormous vogue in China as a cure-all. While grown in the United States for Oriental trade, it is little used in this country. The drug contains an oleoresin, sugar, saponin, and a glucoside, *panaxin*.

Xanthoxylum (U.S.P. IX; N.F. VI), or *Prickly Ash Bark*, is the bark of *Zanthoxylum americanum* (northern prickly ash) and of *Zanthoxylum Clava-Herculis* (southern prickly ash). It contains volatile oil, resin, a bitter principle, *xanthoxylin*; berberin. Xanthoxylin from northern prickly ash is $C_{15}H_{14}O_4$, while that from the southern is $C_{14}H_{12}O_4$.

As in the case of serpentaria, two different plants yield official prickly ash. The constituents of the two barks are practically identical, although it is said that the bitter principle (xanthoxylin) from the two is not exactly the same.

The curious name, xanthoxylum, has a distinct and sensible meaning, and the best way in which to present the matter forcibly is to mention three drugs between whose names there exists a similarity.

These are:

Xanthoxylum, from the Greek "*xanthos*," yellow, and "*xylon*," wood, or yellow wood.

Erythroxylon, from the Greek "*erythros*," red, and "*xylon*," wood, or red wood.

Hæmatoxylon, from the Greek "*haima*," the blood, and "*xylon*," wood, or blood wood.

Xanthoxylin is used as an alterative, diuretic and sialagogue in 2-Gm. doses. The *fluidextract* (p. 271) is recognized by the National Formulary.

Mezereum (N.F. VI), or *Mezereon*, is the bark of *Daphne Mezereum*. It contains acrid resin; wax; daphnin; starch, gum, acids, etc. Daphnin is a glucoside that hydrolyzes to daphnetin. It is used as an irritant, sialagogue and externally as a rubefacient. The drug is a constituent of *compound fluidextract of sarsaparilla*, N.F. *Dose*, 10 grains.

Matico (U.S.P. VIII; N.F. V) represents the dried leaves of *Piper angustifolium* Ruiz and Pavon (Fam. *Piperaceæ*). It contains volatile oil, resin, tannin.

The *volatile oil* consists of terpenes, sesquiterpenes, cineol and phenol ethers (asarone, etc.). As the commercial oil is distilled from leaves of different species of *Piper*, its composition is quite variable. Matico is used as a vulnerary and styptic. Its dose, when taken internally, is 60 grains.

ERIODICTYON—Eriodictyon
(Eriodict.—Yerba Santa)

Eriodictyon is the dried leaf of *Eriodictyon californicum* (Hooker et Arnott) Torrey (Fam. *Hydrophyllaceæ).*
Eriodictyon contains not more than 5 per cent of its stems and not more than 2 per cent of other foreign organic matter.

Constituents.—Resins, trace of volatile oil, tannin, eriodictyol (a phenol), $C_{15}H_{12}O_6$, homo-eriodictyol (a phenol, $C_{16}H_{14}O_6$ and isomeric with hesperetin), 3 per cent; also three other alcohols, *xanthoeridol, eriodonol* and *chrysoeriol.*

Medical Properties.—Expectorant. Chiefly used for masking taste of quinine, *aromatic syrup of yerba santa,* N.F. (p. 223), being generally employed for this purpose. This is prepared from the official *fluidextract* (p. 264).

Dose.—1 Gm. (15 grains).

Grindelia (N.F. VI) represents the leaves and flowering tops of various species of the *Grindelia* genus. It contains volatile oil, fatty acids (formic, cerotic, palmitic, etc., free and as glyceryl esters; a phytosterol, melting at 166° C.; an alcohol $C_{17}H_{28}O_3$, melting at 256° C.; a phenol, $C_{14}H_{12}O_5$, melting at 227° C.; glucose, tannin, etc. It is recommended for asthma. The *fluidextract,* N.F. (p. 271) is also used externally as a lotion in the eruption caused by poison oak. *Dose,* 2 Gm. (30 grains).

Sabina (U.S.P. VIII), or *Savine,* is composed of the tops of *Juniperus Sabina* Linné (Fam. *Coniferæ).* It contains volatile oil, and resin. The natural order *Coniferæ,* to which the savine tree belongs, is commonly called the pine family and yields many important products, as turpentine and Canada turpentine. Savin represents leafy tops, which are the ends of the branches, hence the youngest and freshest part of the trees. It is used as an emmenagogue in 8-grain doses.

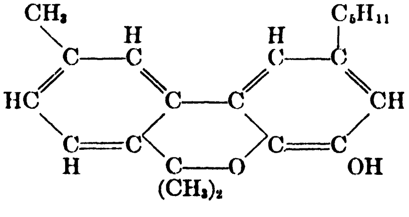
Oleum Sabinæ (U.S.P. VIII), or *Oil of Savine,* is distilled from the fresh tops of savine. It contains *sabinol,* $C_{10}H_{16}O$ (partly as acetic acid ester); *cadinene* and possibly some terpenes. It is used like the drug in 1-minim doses.

CANNABIS—Cannabis
(Cannab.—Cannabis indicæ herba P.I.)

Cannabis consists of the dried flowering tops of the pistillate plants of *Cannabis sativa* Linné (Fam. *Moraceæ).*
It contains not more than 10 per cent of its fruits, large foliage leaves, and stems over 3 mm. in diameter, and not more than 2 per cent of other foreign organic matter. It yields not more than 5 per cent of acid-insoluble ash.

Constituents.—Volatile oil; resin; bitter substance; *cannabine,* an alkaloid.

The *volatile oil* is said by Personne to contain *cannabene,* $C_{18}H_{20}$, while other writers claim it consists of sesquiterpenes. The *resin* called *cannabin* is a mixture, the active ingredient of which is a red oily mixture called *cannabinol,* which is supposed to have the formula:



Remarks.—While formerly only cannabis grown in India was recognized, U.S.P. X permits any cannabis having the potency prescribed by the biological assay. Houghton claims that the American hemp is as active as the Indian if only properly prepared. Marshall claims that the deterioration of the drug is due to the oxidization of cannabinol and that such deterioration can be prevented by keeping the drug hermetically sealed (U.S.P. XI). It gives careful and distinct directions as to assaying the drug biologically.

Medical Properties.—Powerful nervous stimulant, the resinous extract being used in the Far East by smoking, under the name of *hashish.* The *extract,* U.S.P. (p. 299), is largely used to relieve the pain of corns, a favorite recipe for this purpose being *compound salicylic collodion,* N.F. (p. 234). The *fluidextract* (p. 264) is also official.

Dose.—No dose is given in U.S.P. XI. U.S.P. IX dose was 60 mg. (1 grain).

CAPSICUM—Capsicum

(Capsic.—Cayenne Pepper, African Chillies)

Capsicum is the dried ripe fruit of *Capsicum frutescens* Linné (Fam. *Solanaceæ*), grown in Africa.

Capsicum contains not more than 3 per cent of its stems and calyxes, and not more than 1 per cent of other foreign organic matter. It yields not less than 12 per cent of nonvolatile, ether-soluble extractive and not more than 1.25 per cent of acid-insoluble ash.

Constituents.—Volatile oil (trace); resin; fat, *capsaicin.* The oleoresin consists of two oily liquids, *capsicin* and *capsicol,* combined with capsaicin and fat.

Nelson finds that capsaicin is a product of the condensation of vanillyl amine and decenoic acid and is presumably:

$$C_6H_3\left\{\begin{array}{l}OH\\OCH_3\\CH_2NHCOC_9H_{17}.\end{array}\right.$$

Remarks.—Capsicum belongs to the natural order Solanaceæ, the same family of plants to which belongs the Irish potato, the tomato, and the egg-plant; as well as the poisonous drugs, stramonium, belladonna, and hyoscyamus. The official fruit—the pepper pod—is so well known that extended comment is unnecessary. It should be noted that the Pharmacopœia directs a crude ("organoleptic") assay for capsicum.

Medical Properties.—Stimulant, rubefacient, condiment. The *tincture* (p. 246) and *oleoresin* (N.F. VI) (p. 276) are official. From the latter the *ointment* (p. 372) is prepared.

Dose.—Of drug, 60 mg. (1 grain).

Paprika is a special variety of red pepper grown in Hungary and is obtained from *Capsicum annuum.* It is less pungent than the official drug but is more highly colored. The coloring matter is due to *carotin* and *capsanthin.*

Piper (U.S.P. IX; N.F. V), or *Black Pepper,* is the unripe fruit of *Piper nigrum.* It contains volatile oil, resin, *piperin* (p. 904) and its isomere, *chavicin.* The volatile oil contains dipentene, phellandrene and caryophyllene.

Pepper is what is commonly called black pepper, red pepper being given the distinctive name, capsicum. Note that pepper is the unripe fruit, the berry which was picked before fully ripe and shriveled through drying. White pepper represents the same fruit allowed to ripen, after which the fleshy portion is removed by hand, leaving only the seed, with a trace of fruit tissue clinging thereto.

Black pepper is used as an irritant, stimulant, condiment. It is usually administered in tonic pills as *oleoresin* (p. 277).

Dose.—500 mg. (8 grains).

Cubeba (U.S.P. X; N.F. VI), or *Cubebs,* is the dried, nearly full-grown unripe fruit of *Piper cubeba.* It contains volatile oil, 10 to 18 per cent; resin; *cubebic acid; cubebin.*

The latter has the formula, $C_{20}H_{20}O_6$ and is apparently a derivative of piperonal. This drug is an unripe berry, just as is pepper, and from a closely allied plant, both plants belonging to the same genus. It is used as a urinary disinfectant and stimulant. The *oleoresin* (N.F. VI) is used in gonorrhea mixtures, while the *lozenges* (U.S.P. IX) made from the oleoresin are used in bronchitis. The ground drug, smoked as cigarettes, has enjoyed considerable popularity as a remedy for catarrhal troubles. The *fluidextract* (p. 271) and the *tincture* (p. 255) are also recognized by the Formulary. *Dose*, 2 Gm. (30 grains).

Oleum Cubeba (U.S.P. IX), or *Oil of Cubeb*, is the volatile oil distilled from the drug just described. It contains two sesquiterpenes, one of which is cadinene; some terpenes (pinene and dipentene), etc. Old oil contains a sesquiterpene alcohol, $C_{15}H_{26}O$, called cubeb camphor. Oil of cubeb was formerly largely used in conjunction with copaiba (p. 865) dispensed in capsules or in emulsions, for the treatment of gonorrhea; a large number of such preparations being sold by pharmacists. During the last score of years, however, a radical revision of the treatment of gonorrhea has been made by modern medical practitioners and not only have gonorrhea mixtures, capsules and the like lost their vogue in the best informed medical circles but moreover the use of copaiba and cubeb mixtures in the treatment of gonorrhea is deemed improper. This being so, it behooves the pharmacist to discourage the sale of copaiba and cubeb mixtures. Oil of cubeb is given in 8-minim doses.

Humulus (U.S.P. IX; N.F. VI), or *Hops*, are the strobiles of *Humulus Lupulus;* the strobiles being the chaffy scales holding the seed of the plant. The inner surface of the scales contain hairlike appendages called "glandular trichomes" and these "trichomes" constitute the drug, *lupulin*. The medical action of these two drugs is therefore quite similar. Hops contain volatile oil; resins; "hop bitter acids" (*humulone*, $C_{21}H_{30}O_5$; *lupulone*, $C_{26}H_{38}O_4$; and *lactaric* acid, $C_{15}H_{30}O_2$); nitrogenous matter (choline, asparagine, etc.); tannin; sugar, etc.

The resins are combinations of ceryl alcohol and phytosterols with various fatty acids. The volatile oil consists of a sesquiterpene, *humulene*, 66 per cent, *luparone*, $C_{13}H_{22}O$, some olefinic terpenes, oxygenated products, etc.

Hops are used medicinally as a tonic and mild hypnotic, chiefly in domestic practice (hop poultice, etc.). In modern medicine, the more active *lupulin* is usually preferred. Hops are used enormously in beer brewing. The *fluidextract* is recognized in the Formulary. *Dose*, 2 Gm. (30 grains).

Lupulinum (N.F. VI), or *Lupulin*, are the glandular trichomes separated from the strobiles of *Humulus Lupulus*. Their constituents are identical with those of hops and in more concentrated form, and the drug is used like hops in 8-grain doses.

DRUGS CONTAINING VOLATILE OIL, RESIN, AND BITTER PRINCIPLE

Drugs of this class closely resemble those just considered, the only difference being that while in the class just considered the aromatic feature prevailed, the drugs now to be taken are bitter rather than aromatic. The bitter principles found in these drugs have not in most cases been carefully studied.

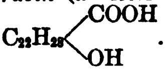
Pyrethrum (U.S.P. IX), or *Pellitory Root*, is obtained from *Anacyclus Pyrethrum*. It contains acrid resin; fixed oil; much inulin; no starch; *pyrethrine* (an alkaloid, $C_{15}H_{27}ON$); pellitorin (a pungent principle, $C_{14}H_{25}ON$). Pellitory scarcely belongs in this class of drugs, as there is no mention in literature as to its containing volatile oil, nor is it strikingly bitter. It is used as a sialagogue and irritant and is said to be efficient in toothache. *Dose*, 2 Gm. (30 grains).

Cypripedium (U.S.P. VIII; N.F. V), or *Lady Slipper Root*, is the rhizome and roots of several species of *Cypripedium*. It contains volatile oil, resins, volatile acid and bitter glucoside, and is used as an antispasmodic in 15-grain doses.

Salvia (N.F. VI), or *Sage*, is the dried leaves of *Salvia officinalis* Linné (Fam. *Labiatæ*). Sage contains volatile oil, tannin, etc. The *volatile oil* consists of thujone, 50 per cent; pinene, salvene, sesquiterpenes, cineol, and borneol. It is used as a carminative, astringent and flavor in 60-grain doses.

Eupatorium (N.F. VI), commonly called *boneset* or *thoroughwort*, is the dried leaves and flowering tops of *Eupatorium perfoliatum* Linné (Fam. *Compositæ*). It contains volatile oil, and a bitter principle, *eupatorin*. It is used as a bitter stomachic in 30-grain doses.

Marrubium (U.S.P. VIII), or *Horehound*, consists of the dried leaves and flowering tops of *Marrubium vulgare* Linné (Fam. *Labiatæ*). It contains volatile oil, resin, *mar-*

rubin (a bitter principle melting at 160° C.), which is the lactone of *marrubic acid*,  $C_{22}H_{28}\left<\begin{matrix}COOH\\OH\end{matrix}\right.$. It is a stimulant, tonic, popular domestic cough remedy. *Dose*, 30 grains.

Echinacea (N.F. VI) consists of the dried rhizomes and roots of *Brauneria pallida* and *B. angustifolia*. These plants grow in the central western states where they have long been used in domestic medicine. The drug contains inulin, protein, sugars, resin and a volatile oil, which contains a tetra-hydro-sesquiterpene, $C_{15}H_{28}$. Echinacea is used as a "blood purifier" in 15-grain doses, by eclectic physicians. Many pharmacologists declare that it is worthless.

Anthemis (U.S.P. VIII), or *Roman Chamomile*, is the dried flower-heads of *Anthemis nobilis* Linné (Fam. *Compositæ*), collected from cultivated plants. This drug, also called *English chamomile*, contains volatile oil, anthemic acid and a glucoside, *anthemidin*. Power and Browning have isolated nine other constituents, among them apigenin, $C_{15}H_{10}O_5$, choline, phytosterols and fatty acids. The volatile oil consists of a mixture of the esters of butyl, amyl, and hexyl alcohols with butyric, tiglic and angelic acids, with a camphor isomere, *anthemol*, and a paraffin, *anthemene*. It is used as a carminative, analgesic, emmenagogue, in 30-grain doses.

Matricaria (N.F. VI), or *German Chamomile*, represents the dried flower-heads of *Matricaria Chamomilla*. The drug contains volatile oil; bitter principle; fat; wax; resin; gum; etc.

The volatile oil consists of the esters of caprylic and nonylic acids and is blue in color. Its color is due to *azulene* (see p. 882). Other constituents of the flowers isolated by Power and Browning were apigenin, umbelliferone, dihydroxy-coumarin and phytosterols. Matricaria is used in 4-drachm doses.

Calendula (U.S.P. VIII; N.F. VI), or *Marigold*, represents the dried ligulate florets of *Calendula officinalis*.

The drug contains volatile oil; resin; fixed oil but no tannin. Calendula belongs to the largest of all plant families, the *Compositæ*, or sunflower family. The type of the family is the sunflower, the large so-called "flower" of which is really a large collection of small flowers arranged in a close cluster or head. An examination of the sunflower will show this: the black, brushlike disk being composed of florets of one sort (the tubular), while the outer row is composed of florets with a large yellow expansion of the petal on one side. As this expansion is somewhat strap-shaped, such little flowers as have them are called ligulate, from the Latin *ligula*, a strap. While the chamomile, like the sunflower and the daisy have both tubular and ligulate florets, calendula consists of ligulate florets only.

Insect Powder, or *Pyrethrum Flowers*, is the powdered flower heads of *Chrysanthemum cinerariæfolia*, a plant that grows in Persia, Dalmatia, and California. The activity of insect powder is said to reside in two principles, *pyrethrin I* and *pyrethrin II*. The latter is 80 per cent more toxic to flies than is the former. These bodies are esters of an alcohol, *pyrethrolon*, $C_{11}H_{16}O_2$, combined with two acids, $C_{10}H_{16}O_2$ and $C_{11}H_{16}O_4$ respectively. The alcohol, *pyrethrol* of earlier investigators, is said to be inactive as an insecticide. The powder, applied either by dusting with a bellows or by burning, is useful in destroying small insects.

Derris, or *Tuba Root*, is the root of *Derris elliptica*, which is used by the natives of the East Indies as a fish stupefier, contains *rotenone*, *deguelin* and toxicarol. Rotenone is a white crystalline substance melting at 163° C. and having the formula, $C_{23}H_{22}O_6$. Derris is now largely used in the manufacture of spray insecticidical preparations.

Cuba, or *Cube*, is the root of a South American plant, *Lonchocarpus nicou*, which is used by the natives as a fish poison. It is now used in this country in the preparation of insecticides.

Arnica (N.F. VI), or *Arnica Flowers*, are the dried flower-heads of *Arnica montana*. Arnica contains volatile oil; resin; *arnicin*; *arnicine*; etc. It is an irritant and vulnerary and is used chiefly externally in the form of the *tincture*, N.F. (p. 255). The Formulary also recognizes the *fluidextract* (p. 270). *Dose*, 0.2 Gm. (3 grains).

Arnica Root (U.S.P. 1890) contains about the same constituents as the flowers and is used for the same purpose.

OLEORESINS AND BALSAMS

In this class we group those drugs which are plant exudations and consist of a mixture of volatile oil and resin (*natural oleoresins*) or of an oleoresin containing benzoic, cinnamic, and other aromatic acids (*balsams*). We have already studied (p. 275) pharmaceutic oleoresins, those bodies prepared by extracting the oil and resins from such plant drugs as we have just considered—*e. g.*, capsicum, cubeb, etc.—by percolation with acetone, ether or alcohol. The oleoresins we will now consider are natural exudations, oozing from trunks of trees through natural fissures or artificial incisions.

Terebinthina (N.F. VI), or *Turpentine,* is a concrete oleoresin obtained from *Pinus palustris* Miller, and from other species of *Pinus* (Fam. *Pinaceæ*). It contains volatile oil, 22.5 per cent; resin, 70 per cent (rosin, U.S.P.). Terebinthina is familiarly and incorrectly called "gum turpentine." Already it has been mentioned that the modern idea of a gum is a substance soluble in water and insoluble in alcohol. As turpentine is insoluble in water and soluble in alcohol, it is clear it should no longer be considered among the "gums."

We will consider rosin in the chapter devoted to resinous bodies, at which time its chemistry will be discussed. Turpentine is a stimulant used almost entirely as a plaster base.

OLEUM TEREBINTHINÆ—Oil of Turpentine

(Ol. Tereb.—Turpentine Oil, "Spirits of Turpentine")

Oil of Turpentine is the volatile oil distilled from the oleoresin obtained from *Pinus palustris* Miller and other species of *Pinus* (Fam. *Pinaceæ*) which yield exclusively terpene oils.

Note.—Rectified Oil of Turpentine is to be dispensed when Oil of Turpentine is required for internal use. Oil that has become turbid must not be dispensed.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless liquid; characteristic odor and taste, which grows stronger on aging; soluble in 5 volumes of alcohol; sp. gr., 0.854 to 0.868; optical activity, variable; refractive index, 1.4680 to 1.4780; on distillation, 90 per cent of the oil passes over between 154° and 170° C. For details, see U.S.P., p. 270.

For *tests for identity* and for *impurities* (fixed oils, mineral oil, petrolatum, paraffin and rosin oils), see U.S.P., p. 269.

Composition.—Chiefly pinene. The American oil is dextrogyrate, while the French oil is levogyrate. Otherwise the two are practically identical.

Remarks.—This represents the average *spirits of turpentine* of commerce. Note that the presence of mineral oil is detected by treatment with fuming sulfuric acid. This chemical destroys most of the oil of turpentine whereas mineral oils are unaffected by such vigorous treatment. Note also that the refractive index figures in the pharmacopœial monograph.

Incompatibilities.—See prescription No. 4 in Chapter LIX.

Medical Properties.—Stimulant, antiseptic, urinary disinfectant. The Pharmacopœia directs that for internal use the *rectified oil* should be employed.

OLEUM TEREBINTHINÆ RECTIFICATUM—Rectified Oil of Turpentine

(Ol. Tereb. Rect.—Rectified Turpentine Oil)

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Condensed Recipe.

Shake oil of turpentine with solution of sodium hydroxide and then distil. Collect about three fourths of the original oil as distillate, separate it from the aqueous distillate, dry it with calcium chloride and then filter. For details, see U.S.P., p. 270.

Summarized Description.

Colorless liquid; sp. gr., 0.853 to 0.862· leaves less than 0.3 per cent residue on evaporation; for other tests, see oil of turpentine.

Remarks.—It will be seen that this represents the commercial oil mixed with alkali and redistilled, and it is thus freed from resinous materials which are present in the crude oil, giving it a disagreeable odor and taste.

Medical Properties.—That of the crude oil. The *emulsion* (p. 287) is official.

Dose.—0.3 cc. (5 minims).

OLEUM PINI PUMILIONIS—Oil of Dwarf Pine Needles

(**Ol. Pin. Pumil.**—Pine Needle Oil)

Oil of Dwarf Pine Needles is the volatile oil distilled with steam from the fresh leaves of *Pinus montana* Miller (*Pinus pumilio* Haenke) (Fam. *Pinaceæ*).

Oil of Dwarf Pine Needles yields not less than 5 per cent of esters calculated as bornyl acetate ($C_{10}H_{17}.C_2H_3O_2$).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Colorless, or faintly yellowish oil; pleasantly aromatic odor; bitter, pungent taste; sp. gr., 0.853 to 0.869; optical rotation, −5 degrees to −12 degrees in a 100-mm. tube; refractive index, 1.4750 to 1.4800; soluble in 4.5 to 8 volumes of 90 per cent alcohol. For details, see U.S.P., p. 265.

For *assay* (esters), see U.S.P., p. 265.

Remarks.—This official oil represents the distillate from the fresh leaves of the dwarf pine.

Oleum templinum on the other hand, is the distillate from the twigs and the cones of *Pinus pumilio;* while *pine wood oil* is the distillate from the "light wood" of *Pinus palustris*. Each of these oils are obtained from its respective source by distillation with steam. The first two are used in inhalers and vaporizers in catarrhal troubles; while pine wood oil is now largely used as a solvent.

Terebinthina Canadensis (U.S.P. VIII), or *Balsam of Fir*, is a liquid oleoresin obtained from *Abies balsamea* (Linné) Miller (Fam. *Coniferæ*). It contains volatile oil, acid resins, and indifferent resins. The *volatile oil* is chiefly levogyrate pinene. The balsam is used as a stimulant and for mounting microscopic specimens, the object being embedded in a hard, transparent varnish after standing.

Terebinthina Laricis, or *Venice Turpentine*, is the oleoresin from *Larix Europaea*, the larch, a tree closely related to the pine. The product sold in American drugstores for "drawing out" splinters saw neither Venice nor the larch tree, but is made by dissolving rosin in oil of turpentine.

PIX PINI—Pine Tar

(**Pix Pin.**—Pix Liquida)

Pine Tar is a product obtained by the destructive distillation of the wood of *Pinus palustris* Miller, or of other species of *Pinus* (Fam. *Pinaceæ*).

Storage.—Preserve in well-closed containers.

Summarized Description.

Semiliquid, viscid, brownish-black noncrystalline liquid; empyreumatic terebinthinate odor; sharp empyreumatic taste; miscible with alcohol, ether, chloroform, glacial acetic acid, fixed and volatile oils; slightly soluble in water, the solution being yellowish to yellow-brown in color.

Constituents.—Volatile oil, U.S.P.; pitch; pyroligneous acid (p. 649).

Remarks.—Tar is made by stacking billets of pine wood on the earth into a conical mound, and setting fire to the wood after covering with plastered earth. Enough air is admitted through holes in the earth covering to permit the wood to smoulder, and a hole at the top of the mound serves as a chimney. Before stacking the wood, radiating ditches are dug on the ground on which the mound is to be built, the ditches running into a circular trench surrounding the mound. The smouldering heat decomposes the wood into smoke (which passes off through the hole in the top of the mound), tar (which runs into the circular trench and is transferred to barrels) and charcoal, which is sacked after the fire is extinguished and the earth covering removed. The process has already been touched upon on pp. 100 and 434.

Medical Properties.—Stimulant and antiseptic. Used for bronchial affections as the official *syrup* (p. 220), which is made from the *rectified oil* (see below), and externally as the official *ointment* (p. 369).

Dose.—500 mg. (8 grains).

Glycerole of Tar is made by mixing washed tar with alcohol, triturating mixture with magnesium carbonate and water, and filtering. It contains the equivalent of 63 Gm. tar to the liter. A simpler recipe consists in mixing 1 fluidounce oil of tar with 2 fluidounces of alcohol, triturating to smooth paste with 6 drachms magnesium carbonate, adding 4 fluidounces glycerin and 4 fluidounces water, macerating several days, and then filtering.

Liquor Picis Alkalinis (N.F. IV) is a solution of pine tar in potassium hydroxide.

OLEUM PICIS RECTIFICATUM—Rectified Oil of Tar

(**Ol. Pic. Rect.**—Oleum Picis Liquidæ Rectificatum)

Rectified Oil of Tar is the volatile oil from pine tar rectified by steam distillation.

Summarized Description.

Thick, dark-reddish-brown liquid; strong empyreumatic odor and taste; soluble in alcohol; sp. gr., 0.960 to 0.990. For details, see U.S.P., p. 265.

Composition.—A vast number of products similar to those obtained in the manufacture of crude pyroligneous acid, such as toluene, xylene, mesitylene, phenol, creosote, naphthalene, etc.

Medical Properties.—Stimulant and antiseptic. Used in making the official *syrup* (p. 220).

Dose.—0.2 cc. (3 minims).

PIX JUNIPERI—Juniper Tar

(**Pix Junip.**—Oleum Cadinum U.S.P. X, Oil of Cade, Oleum Juniperi Empyreumaticum)

Juniper Tar is the empyreumatic volatile oil obtained from the woody portions of *Juniperus Oxycedrus* Linné (Fam. *Pinaceæ*).

Summarized Description.

Dark-brown, clear thick liquid; tarry empyreumatic odor; faintly aromatic, bitter taste; almost insoluble in water; partly soluble in alcohol and in petroleum benzin; completely soluble in ether, amyl alcohol, chloroform, glacial acetic acid and oil of turpentine; sp. gr., 0.950 to 1.055. For details, see U.S.P., p. 292.

For *tests for identity* and for *impurities* (rosin and rosin oil), see U.S.P., p. 292.

Composition.—Phenols, resin, large amount of cadinene.

Remarks.—This is a tarry oil prepared from a species of juniper wood by destructive distillation. The distillation is carried on in a brick kiln, the wood itself, as in the case of tar (p. 863), furnishing the heat.

Medical Properties.—Like tar, chiefly externally.

Coal Tar is a side product in the manufacture of illuminating gas (p. 83). It is described in the National Formulary under the title, *pix carbonis*.

Liquor Picis Carbonis (N.F.) is a solution of coal tar in alcohol, quillaja being used to facilitate solution.

COPAIBA—Copaiba

(Copaib.—Balsam Copaiba)

An oleoresin derived from South American species of *Copaiba* (Fam. *Leguminosæ*).

Summarized Description.

Pale yellow or brownish-yellow viscid liquid; sometimes slightly fluorescent; peculiar aromatic odor; bitter, acrid taste; insoluble in water; partly soluble in alcohol; soluble with some opalescence in dehydrated alcohol and carbon disulfide; entirely soluble in chloroform, ether, and in petroleum benzin; sp. gr., 0.930 to 0.995; acid value, 28 to 95. For details, see U.S.P., p. 130.

For *tests for identity* and for *impurities* (paraffin and fatty oils, Gurjun balsam, paraffin oils, African copaiba), see U.S.P., p. 130.

Constituents.—Volatile oil (80 per cent in best quality), resin (p. 306).

Remarks.—Copaiba has been largely adulterated, hence lengthy tests given in U.S.P. XI. For making mass of copaiba, U.S.P., 1890, samples containing large amounts of resin should be employed, such as the Maracaibo copaiba, which contains only 30 to 40 per cent oil.

Incompatibilities.—See prescription 18 in Chapter LIX.

Medical Properties.—Urinary antiseptic. Popular remedy for gonorrhea, administered in emulsion. The National Formulary gives a recipe for such an emulsion, *Lafayette mixture.* (See p. 280.)

Dose.—1 cc. (15 minims).

Oleum Copaibæ (U.S.P. VIII) is a volatile oil distilled from copaiba. It contains sesquiterpenes (α and β caryophyllenes, cadinene, etc.) and is used like copaiba, in 8-minim doses.

OFFICIAL BALSAMS

Balsams are natural products, differing from oleoresins only in containing benzoic and cinnamic acids, the presence of which give the balsams their delightful odor. As all so-called "gums" are not true gums, even so every substance termed a balsam does not come within the pharmaceutic meaning of that term. For instance, copaiba is not a true balsam, since it contains neither benzoic nor cinnamic acid. It is an oleoresin pure and simple.

BALSAMUM PERUVIANUM—Peruvian Balsam

(Balsam. Peruv.—Balsam of Peru, Peru Balsam)

Peruvian Balsam is obtained from *Toluifera Pereiræ* (Royle) Baillon (Fam. *Leguminosæ*).

Summarized Description.

Viscid dark-brown liquid, free from stringiness or stickiness; transparent reddish-brown in thin layers; agreeable vanilla-like odor; bitter acrid taste; does not harden on exposure to the air; soluble in alcohol, chloroform and glacial acetic acid (sometimes with slight opalescence); partly soluble in ether or petroleum benzin; practically insoluble in water; sp. gr., 1.150 to 1.170; acid number, 56 to 84. For details, see U.S.P., p. 79.

For *tests for identity* and for *impurities* (fixed oils, rosin, turpentine), see U.S.P., p. 79.

Saponification Number.—235 to 238. Details in U.S.P., p. 79.

Constituents.—Volatile oil (called *cinnamein*), 60 per cent; resin, 30 per cent, benzoic and cinnamic acids; vanillin, etc.

The *volatile oil* consists of benzyl alcohol, benzylic benzoate, and benzylic cinnamate. The *resin* yields 66 per cent protocatechuic acid, on fusing with potassium hydroxide, and is an ester of peru-resinol with cinnamic and benzoic acids.

Remarks.—Of the tests given in U.S.P. XI, reference need be made only to the cinnamein assay, which concluded with estimation of its saponification number. "Synthetic" balsam of Peru is now found in the German market.

Incompatibilities.—See prescriptions Nos. 70 and 92 in Chapter LIX.

Medical Properties.—Stimulant, antiseptic. Chiefly externally.

BALSAMUM TOLUTANUM—Tolu Balsam

(Balsam. Tolu.—Tolu U.S.P. X, Balsam of Tolu)

Tolu Balsam is obtained from *Toluifera Balsamum* Linné (Fam. *Leguminosæ*).

Summarized Description.

Yellowish-brown or brown plastic solid; brittle when old or dry or cold; transparent in thin layers; pleasant, aromatic, vanilla-like odor; mild aromatic taste, nearly insoluble in water and in petroleum benzin; soluble in alcohol, chloroform and ether; mostly soluble in solutions of fixed alkalis. For details, see U.S.P., p. 80.

For *tests for identity* and for *impurities* (rosin, rosin oil, copaiba), see U.S.P., p. 80.

Saponification Number.—154 to 220. Details in U.S.P., p. 80.

Acid Number.—112 to 168. Details in U.S.P., p. 80.

Constituents.—Volatile oil; two resins; benzoic and cinnamic acids; benzyl and coniferyl benzoates. The composition of volatile oil not known.

Incompatibilities (of syrup).—See prescription No. 45 in Chapter LIX.

Medical Properties.—Flavor, stimulant, popularly used as an expectorant in the form of the official *syrup* (p. 219), which is made from the official *tincture* (p. 244). A constituent of *compound tincture of benzoin* (p. 245).

STYRAX—Storax

(Liquid Storax)

A balsam obtained from the trunk of *Liquidambar orientalis* Miller, known in commerce as Levant Storax, or of *Liquidambar styraciflua* Linné, known in commerce as American Storax (Fam. *Hamamelidaceæ*).

Summarized Description.

Semiliquid, grayish, sticky opaque mass, depositing on standing a dark-brown stratum (Levant) or semisolid or solid mass softened by warming (American); transparent in thin layers; characteristic odor; acrid taste; insoluble in water; soluble in 1 volume of warm alcohol; mostly soluble in ether, acetone, benzene and carbon disulfide.

For details, see U.S.P., p. 364.

For *tests for identity*, see U.S.P., p. 364.

Acid Number.—Levant, 56 to 85; American, 38 to 85. Details in U.S.P., p. 364.

Saponification Number.—160 to 200. Details in U.S.P., p. 364.

Assay (cinnamic acid).—See U.S.P., p. 364.

Constituents.—Volatile oil; resin; benzoic and cinnamic acids; *styracine* (cinnamate of cinnamyl) and other esters; vanillin; *cinnamene* (or *styrol*), $C_6H_5CH{=}CH_2$.

The *volatile oil* consists of cinnamene, styrocamphene, and esters of cinnamic acid.

Remarks.—Since the World War Levant storax has been very scarce, hence the new Pharmacopœia has included under the heading, "Styrax," the *sweet gum* of the southern United States, which is the exudation from *Liquidambar styraciflua.*

Medical Properties.—Similar to Balsam of Peru. A constituent of *compound tincture of benzoin* (p. 245).

Dose.—1 Gm. (15 grains).

BIBLIOGRAPHY

Perfume Extraction.—(General) Bennett and Hollins, Perf. Ess. Oil Record, 9, 1918, 128; Power, Jl. Ind. Eng. Ch., 11, 1919, 344; Gattefossé, C.A., 16, 1922, 2961. (Expression) Rizzato, Ch. and Dr., 35, 1889, 269; Flückiger, Am. Dr., 19, 1890, 26. (Enfleu-

rage) Anon., Am. Dr., 19, 1890, 130; Rabak, Spatula, 17, 1911, 467 and 531; Floriane-Nivière, C.A., 18, 1924, 2581; Redgrove, Ch. and Dr., 111, 1929, 395 and Ph. Jl., 127, 1931, 286; Trabaud, C.A., 25, 1931, 2240. (Volatile solvent extraction) Jeancard, Am. Perfumer, 2, 1907, 10; Soden, Jl. Soc. Ch. Ind., 44, 1925, 690B; Vinogradova, C.A., 24, 1930, 5934.

Volatile Oils.—(General) Myers and Thienes, Jl. A.M.A., 84, 1925, 1895; Harvey, A.J.P., 100, 1928, 524; Chugaev and Chesno, C.A., 24, 1930, 5933; Miller, A.J.P., 103, 1931, 324.

Oil of Cajuput.—(Constituents) Wallach, A., 225, 1884, 315; Voiry, Comp. rend., 106, 1888, 1538 and Jl. de ph. et ch., 18, 1888, 149; Spoelstra, Jl. Soc. Ch. Ind., 48, 1929, 376B. (Green color) Schosafel, A.J.P., 6, 1834, 348; Duyster, C.A., 20, 1926, 2717.

Oil of Chenopodium.—(Source) Wirth, Jl. A.Ph.A., 9, 1920, 127; Van der Wielen, Ch. and Dr., 93, 1920, 1334; Sullivan, Pharm. Era, 54, 1921, 23; Konantz, Jl. A.Ph.A., 13, 1924, 201; Hogstad, A.J.P., 96, 1924, 809; Rojdestvensky, Jl. Soc. Ch. Ind., 44, 1925, 25B. (Constituents) Garrigues, A.J.P., 26, 1854, 40; Nelson, Jl. Am. Ch. Soc., 33, 1911, 1404; Wallach, A., 392, 1912, 67; Hall and Hamilton, C.A., 13, 1919, 2923; Henry and Paget, Ph. Jl., 107, 1921, 349; Langer, Ph. Week., 58, 1921, 1392; Henry and Paget, Jl. Soc. Ch. Ind., 44, 1925, 606 and 737B; Munch and Reindollar, Jl. A.Ph.A., 20, 1931, 443. (Ascaridol) Thoms and Dobke, C.A., 24, 1930, 2133; Richter and Presting, 25, 1931, 3980; Greene, Jl. A.Ph.A., 20, 1931, 20. (Pharmacology) Salant, J. Pharmacol., 2, 1910, 391; C.A., 9, 1915, 1941; Motter, 87, 1915, 36; Heiser, Jl. A.M.A., 66, 1915, 526; Hall, Walker, Zeigler and others, Yearbook, A.Ph.A., 6, 1917, 340; Roth, Hull and Hamilton, Dr. Circ., 63, 1919, 105; Livingston, C.A., 16, 1922, 3711; Cains, C.A., 18, 1924, 1338 and 1529; Docherty, C.A., 18, 1924, 124; Bliss, Jl. A.Ph.A., 14, 1925, 93; Smillie and Pessôa, Jl. Soc. Ch. Ind., 44, 1925, 114B; Hassan and Salah, Pract. Dr., 49, May, 1931, 34.

Oil of Erigeron.—(Constituents) Power, Ph. Rund., 5, 1887, 201.

Oil of Juniper.—(Constituents) Wallach, A., 227, 1885, 288; Anon., Schimmel's Rep., Oct., 1910, 72; Palazzo and Alinari, C.A., 18, 1924, 3098.

Juniper Berries.—(Constituents) Donath, A.J.P., 45, 1873, 447.

Lavender.—Anon., C.A., 25, 1931, 130.

Oil of Lavender.—(Constituents) Bertram and Walbaum, Jl. prakt. Ch., 45, 1892, 590; Anon., Schimmel's Rep., April, 1898, 31.

Oil of Rose.—(Sources and production) Bowkonski Bey, A.Ph.A., 37, 1884, 594; Pappazoglou, A.Ph.A., 24, 1876, 829; Blondel, Am. Dr., 19, 1890, 170; Martell, C.A., 10, 1916, 2614; Anon., Am. Dr., 65, 1917, 59; Kemper, A.J.P., 92, 1920, 428; Anon., Pharm. Era, 53, 1920, 324; De Lorgnes, Ch. and Dr., 93, 1920, 1629; Anon., Nat. Dr., 59, 1929, 387; Martell, N. Y. Apoth. Ztg., 52, 1931, 57. (Constituents) Bertram and Gildemeister, Jl. prakt. Ch., 49, 1894, 185; Hesse, Jl. prakt. Ch., 50, 1894, 472; Tiemann and Schmidt, B., 29, 1896, 922; Soden and Rojan, B., 34, 1901, 2803; Soden and Treff, B., 37, 1904, 1094; Fluckiger, Ph. Jl., [2], 10, 1868, 147; Anon., Schimmel's Rep., April, 1898, 40 and April-May, 1901, 49; Elze, J. Soc. Ch. Ind., 39, 1919, 43A; Anon., Pharm. Era, 54, 1921, 447; Hjort and Eagen, C.A., 14, 1920, 1161.

Oil of Rosemary.—(Constituents) Gildemeister and Stephan, Arch. d. Pharm., 235, 1897, 585; Weber, A., 238, 1887, 89; Bruylants, Jl. de ph. et ch., 29, 1879, 508.

Oil of Santal.—(History) Bode, Ap. Zt., 24, 1909, 17. (Constituents) Semmler and Zaar, B., 43, 1910, 1893; Semmler, B., 40, 1907, 3101 and 3321; Ruzicka and Liebl, C.A., 20, 1926, 1227; Cajola, C.A., 25, 1930, 1636.

Oil of Thyme.—(Constituents) Lallemand, Comp. rend., 37, 1853, 498; A., 101, 1857, 119 and 102, 1857, 119; Anon., Schimmel's Rep., Oct., 1894, 56.

Valerian.—(History) Grier, Am. Dr., 59, 1929, 279. (Constituents) Trommsdorff, Jl. de Ph., 1, 1809, 209; A., 10, 1834, 213; Peters, Ap. Zt., 24, 1909, 537; Oliviero, Comp. rend., 117, 1893, 1096; Haller, Comp. rend., 103, 1886, 151; Goris and Vischinak, Jl. Soc. Ch. Ind., 40, 1921, 409A; Asahina and Hongo, C.A., 18, 1924, 2510; Bullock, C.A., 18, 1924, 3449 and Ph. Jl., 117, 1926, 152 and 210; Madsen, C.A., 22, 1928, 4720.

The Viburnums.—(Botany) Farwell, Bull. Pharm., 27, 1913, 65 and N.W. Dr., 27, 1919, 245; Sayre, A.J.P., 67, 1895, 387; Hommell, Pract. Dr., 43, May, 1925, 26; Youngken, Jl., A.Ph.A., 19, 1930, 680; 20, 1931, 315 and 21, 1932, 444; Peyer and Gstirner, C.A., 26, 1932, 253. (Constituents) Monroe, A.J.P., 18, 1846, 55; Van Allen, A.J.P., 52, 1880, 439; Heyl, Jl. Am. Ch. Soc., 42, 1920, 1744 and Jl. A.Ph.A., 11, 1922, 329.

Sassafras.—(History and constituents) Procter, A.J.P., 38, 1866, 481. (Constituents) Reinsch, A.J.P., 18, 1847, 159.

Oil of Sassafras.—(Constituents) Power and Kleber, Ph. Rev., 14, 1896, 101.

The Cinnamons.—(History) Ruschenberger, A.J.P., 10, 1838, 32; Anon., A.J.P., 34, 1862, 434; Schoff, Jl. Am. Oriental Soc., 42, 1920, 261; LaWall, A.J.P., 95, 1923, 219; Redgrove, Ph. Jl., 123, 1929, 167. (Constituents) Vauquelin, Jl. de Ph., 3, 1817, 433.

Oil of Cassia.—(Constituents) Dumas and Peligot, A., 12, 1834, 24; 13, 1835, 76; 14, 1835, 50; Bertram and Kuersten, Jl. prakt. Ch., 51, 1895, 316; Anon., Schimmel's Rep., Oct., 1889, 19; Dodge and Sherndal, Jl. Ind. Eng. Ch., 7, 1915, 1055. (Source) Anon., Ph. Jl., [3], 20, 1890, 749. (Impurities) Hirschsohn, Am. Dr., 21, 1892, 64. (Medical uses) Plant and Miller, C.A., 17, 1923, 3544.

Eucalyptus.—(Constituents) Cloez, Jl. de ph. et ch., [4], 12, 1870, 201; Atterberg, B., 9, 1876, 316.

Oil of Eucalyptus.—(Constituents) Cloez, A., 154, 1870, 372; Jahns, B., 17, 1884, 2941; Wallach and Gildemeister, A., 246, 1888, 283; Penfold and Simonsen, Jl. Soc. Ch. Ind., 48, 1929, 1112.

Buchu.—(Source) Mathews, Ph. Jl., 107, 1921, 308. (Constituents) Jones, A.J.P., 51, 1879, 198; Flückiger, Ph. Jl., [3], 11, 1880, 174 and 219; Spica, Ph. Jl., 16, 1885, 106; Kondakow, Jl. prakt. Ch., 54, 1896, 433; Shimoyama, Arch. d. Pharm., 226, 1888, 403; Wallach and Weissenborn, Jl. Soc. Ch. Ind., 43, 1924, B447; von Auers, C.A., 18, 1924, 3371; Oesterle and Wander, C.A., 20, 1926, 391.

Hedeoma.—(Constituents) Kremers, A.Ph.A., 35, 1887, 546; Hayne, A.J.P., 63, 1891, 477.

Oil of Hedeoma.—(Distillation) Kremers (above); Bennett, A.Ph.A., 55, 1907, 877. (Constituents) Kremers (above); Barrowcliffe, Jl. Ch. Soc., 91, 1907, 875; Genovesse, A.Ph.A., 53, 1905, 751; Bennett, C.A., 13, 1919, 247. (Pharmacology) Macht, C.A., 7, 1913, 3367.

Peppermint.—(Constituents) Pereira, Materia Medica, 2, 1854, 446.

Oil of Peppermint.—(Source and production) Russell, Spatula, 27, 1921, 481 and Jl. A.Ph.A., 15, 1926, 566. (Constituents) Power and Kleber, Ph. Rund. 12, 1894, 157; Braun, A.J.P., 102, 1930, 202.

Spearmint.—(Constituents) Pereira, Materia Medica, 2, 1854, 444.

Oil of Spearmint.—(Constituents) Flückiger, B., 9, 1876, 473; Trimble, A.J.P., 57, 1885, 484; Schreiner and Kremers, Ph. Rev., 14, 1896, 244; Nelson, C.A., 6, 1912, 1041.

Clove.—(History) LaWall, A.J.P., 95, 1923, 220; Roddis, Jl. A.Ph.A., 19, 1930, 250; Redgrove, Ph. Jl., 123, 1929, 368. (Constituents) Bonastre, Jl. de Ph., 11, 1825, 103; 13, 1827, 464, and 20, 1834, 565; Mylius, Arch. d. Pharm., 203, 1873 392; Swain, A.Ph.A., 36, 1888, 380; Dodge, J. Am. Ch. Soc., 40, 1918, 1917 and 52, 1930, 1722.

Oil of Clove.—(Constituents) Bonastre (see above); Wallach, A., 271, 1892, 287; Masson, Comp. rend., 149, 1909, 630 and 795.

Anise.—(History) LaWall (see above). (Constituents) Stern, Zt. angew. Ch., 6, 1893, 137. (Adulteration) Anon., A.J.P., 33, 1861, 408.

Oil of Anise.—(Constituents) Buchner, Rep. f. Pharm., 15, 1823, 63; Landolph, A.Ph.A., 24, 1876, 281; Anon., Schimmel's Rep., Oct., 1895, 7; Mareeuw, C.A., 20, 1926, 3208; Rutovskii and Leonov, C.A., 23, 1929, 239; Takens, Jl. Soc. Ch. Ind., 48, 1929, 910B; Duncan and co-workers, *ibid.*, 51, 1932, 128B.

Coriander.—(Constituents) Stern (see above).

Oil of Coriander.—(Constituents) Anon., Schimmel's Rep., Oct., 1909, 47. (Physical constants) Grimme, Ph. Cent., 52, 1911, 667.

Fennel.—(Constituents) Stern (see above).

Oil of Fennel.—(Constituents) Blanchet and Sell, A., 6, 1833, 287; Wallach and Hartmann, A., 259, 1890, 324 and 263, 1891, 129; Rutovski and co-workers, Jl. Soc. Ch. Ind., 47, 1928, 768B.

Caraway.—(History) LaWall, A.J.P., 95, 1923, 219. (Constituents) Trommsdorff, A., 3, 1832, 285.

Oil of Caraway.—(Constituents) Wallach, A., 227, 1885, 291 and 277, 1893, 107.

Pimenta.—(History) LaWall (see above). (Constituents) Bonastre, Jl. de Ph., 11, 1825, 187 and 13, 1827, 466.

Oil of Pimenta.—(Constituents) Oeser, A., 131, 1864, 277.

Cardamom.—(History) LaWall, A.J.P., 95, 1923, 219. (Pharmacognosy) Otte and Weiss, Ph. Zent., 69, 1928, 613. (Constituents) Stern, Zt. angew. Ch., 6, 1893, 137; Weber, A., 238, 1887, 98; Anon., Schimmel's Rep., Oct., 1897, 11; Moudgill, C.A., 18, 1924, 2222. (Properties) Parry, Ph. Jl., 63, 1889, 105.

Sabal.—(Constituents) Schreiner, Ph. Rev., 18, 1900, 217; Sherman and Briggs, Pharm. Arch., 2, 1899, 101; Mann, Pharm. Era, 49, 1916, 89; Vanderkleed and Ewe, Jl. A.Ph.A., 5, 1916, 720.

Citrus Fruit.—(History) Rognetta, Am. Dr., 68, Nov., 1920, 29. (Biology) Ajon, C.A., 21, 1927, 757.

Bitter Orange Peel.—(Constituents) Tanret, Ph. Jl., 16, 1886, 839; Tiemann, B., 14, 1881, 970; Tunmann, Ph. Cent., 56, 1915, 135; Oesterle and Kueny, Arch. Pharm., 253, 1915, 383; King and Robertson, C.A., 25, 1931, 5430; Rovesti, C.A., 25, 1931, 2522.

Sweet Orange Peel.—(Constituents) Lebreton, Jl. de Ph., 14, 1828, 377; Helger, B., 9, 1876, 26; Hoffmann, B., 9, 1876, 685; Hall, Jl. Am. Ch. Soc., 47, 1925, 1191; Matlack, A.J.P., 100, 1928, 599 and Jl. A.Ph.A., 18, 1929, 24; Zechmeister and Tuzson, C.A., 25, 1931, 3377.

Oil of Orange Peel.—(Constituents) Wallach, A., 227, 1885, 289; Semmler, B., 24, 1891, 202; Parry, Ch. and Dr., 56, 1900, 462; Dowzard, A.J.P., 80, 1908, 474. (Extraction) de Villiers, C.A., 25, 1931, 2241. (Preservation) LaWall, A.Ph.A., 58, 1910, 1121.

Lemon Peel.—(Source) Hommell, Pract. Dr., 38, Nov., 1920, 20. (Constituents) Cogswell, A.J.P., 26, 1854, 553; Hoffmann (see above); Willimott and Wokes, Ph. Jl., 115, 1925, 225.

Oil of Lemon.—(Manufacture) Flückiger, Arch. d. Pharm., 227, 1889, 1065; Anon., C.A., 9, 1915, 1970 and 2688; Ungerer, Sutton and Baker, C.A., 17, 1923, 1530; La Face, Jl. Soc. Ch. Ind., 50, 1931, 318B; Romeo, Jl. Soc. Ch. Ind., 44, 1925, 863B and 51, 1932, 1055B; Bennett and Tarbert, C.A., 26, 1932, 3328; Elze, Jl. Soc. Ch. Ind., 45, 1926, 803B; de Villiers, C.A., 25, 1931, 4972. (Constituents) Wallach, A., 227, 1885, 290; Semmler, B., 24, 1891, 203; Doebner, B., 27, 1894, 352; Anon., Schimmel's Rep., Oct., 1897, 26; Umney and Swinton, Ph. Jl., 61, 1898, 196 and 370; Anon., Schimmel's Rep., Oct., 1909, 62.

Oil of Neroli.—(Constituents) Romeo, C.A., 17, 1923, 2476.

Oil of Bergamot.—La Face, C.A., 25, 1931, 4658; Herold, Jl. Soc. Ch. Ind., 50, 1931, 318B.

Myristica.—(History) Redgrove, Ph. Jl., 127, 1931, 184. (Constituents) Bonastre, Jl. de Ph., 9, 1823, 281; Stern, Zt. angew. Ch., 6, 1893, 137; Power and Salway, Jl. Ch. Soc., 91, 1907, 2037; 93, 1908, 1653. Tschirch and Schlowsky, Arch. Pharm., 253, 1915, 102; Bomer and Ebach, C.A., 23, 1929, 818; Collin and Hilditch, Jl. Soc. Ch. Ind., 49, 1930, 141T; Heiduschka and Hübel, Arch. Pharm., 271, 1933, 56.

Oil of Myristica.—(Constituents) Power and Salway (see above); Wallach, A., 252, 1889, 105.

Myristicin.—Structure) Semmler, B., 24, 1891, 3818; Thomas, B., 36, 1903, 3451; Redgrove, Ph. Jl., 127, 1931, 186. (Pharmacology) Power and Salway, A.J.P., 80, 1908, 563.

Mace.—Tschirch and Schklowsky, Arch. Pharm., 253, 1915, 102.

Stillingia.—(Constituents) Saunders, A.Ph.A., 16, 1868, 460; Harmanson, A.J.P., 54, 1882, 386; Bichy, A.J.P., 57, 1885, 529; Miller, Brooks and Rutledge, Jl. A.Ph.A., 4, 1915, 445.

Sumbul.—Reinsch and Buchner, A.J.P., 16, 1844, 119; Reinsch and Riekher, A., 68, 1848, 341; Heyl and Hart, Jl. Am. Ch. Soc., 38, 1916, 432.

Aspidium.—(Constituents) Bock, A.J.P., 24, 1852, 61; Luck, Ch. Cent., 22, 1851, 657 and 676; Grabowsky, Ch. Cent., 38, 1867, 469; Daccoma, A.J.P., 61, 1889, 144; Ehrenberg, Arch. d. Pharm., 231, 1893, 345; Bohm, A., 329, 1903, 286; Karrer and Widmer, Helv. Ch. Acta, 3, 1920, 392; Greene, Jl. A.Ph.A., 20, 1931, 23. (Pharmacology) Miyasaki, Ph. Jl., 126, 1931, 79.

Ginger.—(Constituents) Thresh, A.Ph.A., 28, 1880, 83; 31, 1883, 257 and 33, 1885, 257; Ph. Jl., [3], 12, 1881, 243; Gane, Ph. Jl., [3], 22, 1892, 802; Bertram and Walbaum, Jl. prakt. Ch., 49, 1894, 18; Stenhouse and Groves, A.Ph.A., 26, 1878, 193; Brooks, Jl. Am. Ch. Soc., 38, 1916, 430; Nomura, Yearbook, A.Ph.A., 6, 1917, 199 and 8, 1919, 231; Grier, Ph. Jl., 99, 1917, 172, 205 and 216; Mondgill, C.A., 22, 1928, 4203; Valenzuela and Kremers, Pract. Dr., 47, Sept., 1929, 33; Anon., Ph. Era, 67, 1930, 278. (Pharmacology) Emig, Jl. A.Ph.A., 20, 1931, 114.

Orris.—(Sources) Anon., Ph. Era, 67, 1930, 273; Rovesti, C.A., 26, 1932, 3072. (Constituents) Langlais and Goby, C.A., 18, 1924, 3678; Baker, C.A., 22, 1928, 2356.

Calamus.—(Constituents) Griffith, A.J.P., 5, 1833, 265; Faust, Arch. d. Pharm., 181, 1867, 214; Thomas, Arch. d. Pharm., 224, 1886, 465; Kurbatow, A., 173, 1874, 4; Thoms and Bechstrom, B., 34, 1901, 1021 and 35, 1902, 3187; Russell, Jl. Am. Ch. Soc., 37, 1915, 2387.

Leptandra.—(Constituents) Power and Rogerson, Jl. Ch. Soc., 97, 1910, 1944.

Cimicifuga.—(History) Lloyd, A.Ph.A., 59, 1911, 217. (Constituents) Finnemore, A.Ph.A., 58, 1910, 195.

Serpentaria.—(Constituents) Serullas, Jl. de Ph., 6, 1820, 571; Peacock, A.J.P., 63, 1891, 257; Ferguson, A.J.P., 59, 1887, 481.

Xanthoxylum.—(Constituents) Staples, A.J.P., 1, 1829, 163; Griffith, A.J.P., 8, 1836, 195; Eberhardt, A.J.P., 72, 1890, 231; Gordin, Jl. Am. Ch. Soc., 28, 1906, 1649.

Mezereum.—(Description) Squire, Ph. Jl., 1, 1842, 395. (Constituents) Gmelin and Bär, through Berzelius' Traité de Chimie, 3, 1839, 116; Zwenger, A., 115, 1860, 1.

Matico.—(Description) Dierbach, A., 20, 1836, 266. (Constituents) Hodges, A.J.P., 18, 1847, 178; Niegans, A.J.P., 18, 1847, 174; Thoms, Arch. d. Pharm., 247, 1909, 591.

Yerba Santa.—(Constituents) Mohr, A.Ph.A., 27, 1879, 736; Power and Tutin, Proc. A.Ph.A., 54, 1906, 352 and Proc. Ch. Soc. Lond., 23, 1907, 133 and 243; Jl. Ch. Soc., 91, 1907, 887; 95, 1909, 81; 97, 1910, 2054; Oesterle, Arch. Pharm., 253, 1915, 383; C.A., 13, 1919, 1361; Shriner and Kleiderer, Jl. A.Ph.A., 51, 1929, 1267. (Uses) Hartz, Am. Dr., 15, 1886, 41; Stevens, A.Ph.A., 36, 1888, 89; Eschenbrenner, Ph. Zt., 74, 1929, 93.

Ginseng.—Wong, Jl. A.Ph.A., 10, 1921, 431; Kotake, C.A., 25, 1931, 3439.

Grindelia.—(Constituents) Power and Tutin, A.Ph.A., 53, 1905, 193.

Savin.—(Constituents) Needles, A.J.P., 13, 1841, 41.

Oil of Savin.—(Composition) Fromme, B., 31, 1898, 2025; Wallach, A., 238, 1887, 82.

Cannabis.—(History) Anon., Ch. and Dr., 110, 1929, 41. (Description) Anon., Ph. Jl., 1, 1842, 489. (Constituents) Schlesiger, Buchner's Repert, 21, 1840, 190; Smith, Ph. Jl., 6, 1846, 171; Personnes, Jl. de ph. et ch., 31, 1857, 48; Robiquet, Jl. de ph. et ch., 31, 1857, 46; Humphrey, Ph. Jl., 68, 1902, 342; Marshall, A.Ph.A., 51, 1903, 804; Smith, A.J.P., 63, 1891, 38; Bombelon, Am. Dr., 13, 1884, 132; Valente, B., 13, 1880, 2431 and 14, 1881, 1717; Cahn, C.A., 24, 1930, 4015. (American cannabis) Houghton and Hamilton, A.Ph.A., 55, 1907, 445. (Deterioration) Marshall, Dr. Circ., 53, 1909, 518. (Hashisch) Ball. Therap. Gaz., 34, 1910, 777.

Capsicum.—(Source) Redgrove, Ph. Jl., 128, 1932, 47. (Constituents) Taylor, A.J.P., 29, 1857, 303; Thresh, Ph. Jl., [3], 7, 1876, 21 and 259; Pabst, Arch. d. Pharm., 230, 1892, 108; Buchheim, A.Ph.A., 22, 1874, 106; Nelson, Jl. Am. Ch. Soc., 41, 1919, 1115 and 42, 1920, 597; Lapworth and Royle, Jl. Soc. Ch. Ind., 38, 1919, 843A; Cholnoky, C.A., 25, 1931, 3432 and 4888. (Organoleptic test) Wirth and Gathercoal, Jl. A.Ph.A., 13, 1924, 217.

Pepper.—(History) "X-rayser," Ch. and Dr., 84, 1914, 493. (Constituents) Poutel, Jl. de Ph., 7, 1821, 373; Buchheim, A.J.P., 48, 1876, 467; Eberhardt, Arch. d. Pharm., 225, 1887, 515; Anon., Schimmel's Rep., Oct., 1890, 49; Kremers and Schreiner, Ph. Arch., 4, 1901, 61; Ott, C.A., 17, 1923, 1074 and 18, 1924, 1847; Staudinger and Schneider, Jl. Soc. Ch. Ind., 42, 1923, 273A. (White pepper) Parry, 79, 1911, 167.

Cubeb.—(Constituents) Vauquelin, Jl. de Ph., 6, 1820, 309; Monheims, A.J.P., 18, 1846, 168; Schmidt, A.J.P., 42, 1870, 222; Schulze, Arch. d. Pharm., 202, 1873, 388; Mameli, C.A., 7, 1913, 1722. (Cubebin) Pauly and co-workers, C.A., 19, 1925, 265; Mameli, Gazz. ch. Ital., 42, 1912, 546 and 551; *ibid.*, 51, 1921, 363; Bogert and Powell, Jl. Am. Ch. Soc., 53, 1931, 1607.

Oil of Cubeb.—(Composition) Wallach, A., 238, 1887, 78; Oglialoro, B., 8, 1875, 1357. (Cubeb camphor) Schmidt, B., 10, 1877, 188; Schaer and Wyss, Arch. d. Pharm., 206, 1875, 316.

Eupatorium.—(Constituents) Peterson, A.J.P., 23, 1851, 206; Bickley, A.J.P., 26, 1854, 495; Latin, A.J.P., 52, 1880, 392.

Marrubium.—(History) Leclerc, C.A., 13, 1919, 498. (Constituents) McMaken, A.J.P., 17, 1845, 1; Gorlin, Jl. Am. Ch. Soc., 30, 1908, 265.

The Chamomiles.—Redgrove, Ph. Jl., 122, 1929, 50.

Anthemis.—(Constituents) Amerman, A.J.P., 61, 1889, 69; Power and Browning, Ch. and Dr., 85, 1914, 376; Fittig and Kopp, V., 9, 1876, 195 and 10, 1877, 53; Fittig and Köbig, A., 195, 1879, 79; Massera, Dr. Circ., 65, 1921, 302; Reeb, C.A., 18, 1924, 1847.

Matricaria.—(Constituents) Gerhardt, Ph. Jl., [2], 3, 1862, 429; Herberger and Damur, A., 8, 1833, 231; Hartwich and Jama, A.Ph.A., 58, 1910, 302; Henderson, Ph. Jl., 81, 1908, 683; Power and Browning, Jl. Ch. Soc., 105, 1914, 2280; Massera, Dr. Circ., 65, 1921, 302; Rom, C.A., 25, 1931, 2518; Bergmann, Jl. Soc. Ch. Ind., 50, 1931, 135B. (Pharmacology) Junkmann and Wiechowski, C.A., 23, 1929, 5237.

Calendula.—(Constituents) Geiger, through Berzelius' Traité de Chimie, 3, 1839, 153; Tielke, A.J.P., 63, 1891, 477.

Echinacea.—Sayre, Dr. Circ., 42, 1898, 124; Heyl and Staley, A.J.P., 86, 1914, 451; Kremers and Woods, Jl. A.Ph.A., 18, 1929, 733; Woods, A.J.P., 102, 1930, 611.

Hops.—(Constituents) Power, Tutin and Rogerson, Jl. Ch. Soc., 103, 1913, 1267; and Proc. Ch. Soc., 29, 1913, 180; Chapman, Jl. Ch. Soc., 67, 1895, 54 and 780, 83, 1903, 505 and Ch. and Dr., 84, 1914, 980; Semmler and Mayer, B., 44, 1911, 2009; Wiegmann and Seibriger, C.A., 8, 1914, 2026; Wöllmer, *ibid.*, 13, 1919, 495; Leurs and Baumann, Jl. Soc. Ch. Ind., 39, 1920, 498A; Pyman, Rogerson and Walker, C.A., 17, 1923, 1859; Windisch and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 49B; Wieland and co-workers, C.A., 20, 1926, 744; Wöllmer, C.A., 19, 1925, 2042; Walker, C.A., 19, 1925, 1613; Chapman, C.A., 22, 1928, 2934 and 24, 1930, 1467. (Evaluation) Wöllmer, Jl. Soc. Ch. Ind., 44, 1925, 142B. (Pharmacology and antiseptic value) Walker, Jl. Soc. Ch. Ind., 44, 1925, 1005B; Windisch and co-workers, C.A., 20, 1926, 218; Steidle, C.A., 26, 1932, 2787; Kolbach, Jl. Soc. Ch. Ind., 44, 1925, 372B.

Pyrethrum.—(History) Anon., Nat. Dr., 59, 1929, 500. (Constituents) Koehn, A.J.P., 1836, 175; Schneegans, A.Ph.A., 45, 1897, 736; Staudinger and Ruzicka, Helv. Chim. Acta, 7, 1924, 177, 212 and 377; Yamamoto and Sumi, C.A., 18, 1924, 3169; Ott and Behr, C.A., 22, 1928, 385; Gulland and Hopton, C.A., 24, 1930, 2544.

Insect Powder.—Grieb, A.Ph.A., 56, 1908, 211; Fujitani, *ibid.*, 58, 1910, 191; Sato, Ph. Jl., 82, 1909, 88 and Yearbook, A.Ph.A., 8, 1919, 238; Seidler, *ibid.*, 4, 1915, 119; Chevalier, Mercier and Juillet, C.A., 17, 1923, 3373; Staudinger and Ruzicka, Jl. Soc. Ch. Ind., 43, 1924, B398. (Cultivation) Gnadinger and Corl, Jl. Am. Ch. Soc., 52, 1930, 680; Perrot, C.A., 24, 1930, 4584; Glassford, C.A., 25, 1931, 1621. (Constituents) Gnadinger and Corl, Jl. Am. Ch. Soc., 51, 1929, 3054 and 52, 1930, 3300; Chevalier and Mercier, Dr. Circ., 73, 1929, 247; Anon., A.J.P., 102, 1930, 164. (Evaluation) Tattersfield, C.A., 23, 1929, 5538 and 26, 1932, 3821; McDonnell and co-workers, C.A., 24, 1930, 4887; Vollmar, Jl. Ind. Eng. Ch., Anal. Ed., 3, 1931, 110.

Derris Root and Rotenone.—Clarke, Science, 70, 1929, 478; 71, 1930, 396; 73, 1931, 17; Jl. Am. Ch. Soc., 52, 1930, 2461; 53, 1931, 313 and 729; Butenandt, C.A., 26, 1932, 3253 and 3796; Roark, Pamph. 190, U. S. Dept. Agric., 1932, 1–85.

Cypripedium.—(Constituents) Blair, A.J.P., 38, 1866, 494; Beshore, A.J.P., 59, 1887, 395.

Sage.—(General) Anon., Ch. and Dr., 111, 1929, 463; Waldeck, C.A., 23, 1929, 476; (Constituents) Ilish, through Berzelius' Traité de Chimie, 3, 1839, 147; Muir, Ph. Jl., [3], 7, 1876, 265; Wallach, A., 227, 1885, 280; 252, 1889, 103 and 286, 1895, 93; Anon., Schimmel's Rep., Oct., 1895, 42; Morani, Jl. Soc. Ch. Ind., 48, 1929, 622B. (Medical uses) Schelenz, C A., 23, 1929, 932.

Arnica.—(Constituents) Walz, A.J.P., 33, 1861, 450; Börner, A.Ph.A., 1893, 637.

Turpentine.—(Gathering) Herty, U. S. Dept. Agr. Forest Service, Bull. No. 90; Veitch and Grolisch, Jl. Soc. Ch. Ind., 40, 1921, 165R. (Constituents) Kremers, Ph. Rund., 13, 1895, 135. (Foreign turpentines) Tschirch and students, A.Ph.A., 49, 1901, 744.

Oil of Turpentine.—(Composition) Kremers, Ph. Rund., 13, 1895, 135; De Voy, Ch. Cent., 74, 1867, 304. (Purification) Szigethy, A.Ph.A., 45, 1897, 638; Robinson, C.A., 7, 1913, 2449; Gérard, Jl. Soc. Ch. Ind., 44, 1925, 179B; Dupont and Barraud, *ibid.*, 49, 1930, 248B. (Properties) Ronchesne, C.A., 23, 1929, 4017. (Pharmacology and toxicology) Kunz-Krause, C.A., 22, 1928, 3697. (Ozonized) Blomen, A.J.P., 87, 1915, 199 and 398.

Pine Needle Oil and Oleum Templinum.—Morel, Ph. Jl., [3], 8, 1877, 726; Anon., Schimmel's Rep., April, 1900, 79, and April, 1910, 91; Ludy, A.Ph.A., 56, 1908, 336.

Pine Wood Oil.—Teeple, Jl. Am. Ch. Soc., 30, 1908, 412.

Canada Turpentine.—(Constituents) Morel, Ph. Jl., [3], 8, 1877, 22; Emmerich, A.J.P., 67, 1895, 135; Tschirch and Bruning, Arch. D. Pharm., 238, 1900, 487.

Venice Turpentine.—(Constituents) Morel, Ph. Jl., [3], 8, 1877, 21; Andes, C.A., 6, 1912, 2853.

Tar.—(Preparation and properties) Dunwody, A.J.P., 61, 1880, 600. (Constituents) Stroem, Arch. d. Pharm., 237, 1899, 525.

Birch Tar.—(Constituents) Hlasiwetz, A., 106, 1858, 339; Gorup-Besanez, A., 143, 1867, 129; Tiemann and Koppe, B., 14, 1881, 2005; Tishchenko and co-workers, C.A., 24, 1930, 5145.

Glycerite of Tar.—Wiegand, A.J.P., 56, 1881, 8.

Liquor Picis Carbonis.—Raubenheimer, A.Ph.A., 57, 1909, 131.

Oil of Tar.—(Composition) Stroem (see above).

Oil of Cade.—(Preparation) Planchon, Schw. Wsch. Ch. u. Ph., 59, 1912, 166. (Composition) Troeger and Feldmann, Arch. d. Pharm., 236, 1898, 692; Wallach, A., 238, 1881, 82 and 271, 1892, 297; Huerre, Jl. ph. ch., 19, 1919, 33 and 65; Pritzker and Junkkunz, Schw., Ap. Zt., 59, 1921, 145 and 162; Anon., Ph. Jl., 107, 1921, 166; Massy, C.A., 16, 1922, 4006.

Copaiba.—(History) Anon., Ph. Era, 63, Dec. 11, 1926, 35. (Constituents) Procter, A.J.P., 22, 1850, 289; Maisch, A.J.P., 35, 1863, 17; Strauss, A., 148, 1868, 148. (Tests) Deussen, Arch. d. Pharm., 252, 1914, 590.

Oil of Copaiba.—(Composition) Deussen and Hahn, Ch. Zt., 34, 1910, 872; Anon., Schimmel's Rep., Oct., 1910, 185.

Balsam of Peru.—(Preparation) Anon., Pharm. Era, 53, 1920, 210. (Constituents) Trog. Arch. d. Pharm., 232, 1894, 70; Thoms, A.Ph.A., 48, 1900, 649; Kraut, A., 153, 1870, 129; Kaehler, B., 2, 1869, 512; Bennett, C.A., 23, 1929, 932; Rollett and Schneider, C.A., 24, 1930, 3019. (Synthetic balsam) Anon., A.Ph.A., 56, 1908, 238.

Balsam of Tolu.—(Constituents) Kopp, Jl. de ph. et ch., 11, 1847, 425; Scharling, A., 97, 1856, 71; Busse, B., 9, 1876, 833.

Storax.—(Constituents) Bonastre, A.J.P., 4, 1832, 210; Scharling, A., 97, 1856, 90; Miller, A., 188, 1877, 184; Laubenheimer, A., 164, 1872, 289; Van't Hoff, B., 9, 1876, 5. (Properties) Anselmino, C.A., 20, 1926, 3773.

American Storax.—Jordan, Jl. Ind. Eng. Ch., 9, 1917, 770; Watermeyer, Dr. Circ., 63, 1919, 445; Anon., Pharm. Era, 52, 1919, 313; Mahood and Gerry, Dr. Circ., 65, 1921, 3; Spokes, C.A., 15, 1921, 3723.

CHAPTER XLVIII

RESINS AND NEUTRAL PRINCIPLES

This chapter deals with plant principles, of which less is known than any other group of chemical substances—in truth, the only reason why these bodies are grouped into this chapter is that they have not been sufficiently studied to know to what classes of chemicals they belong, and as its composition is worked out, each body will be placed in its appropriate position in systematic chemistry, leaving nothing for discussion in this chapter.

This work is already begun. It is now known that resin of jalap owes its activity to the glucoside, convolvulin; while resin of scammony is active because of its glucoside, scammonin; therefore, these two so-called "resins" are considered among the glucosidal drugs.

The phrase "resin acid" is here used in the attempt to classify the important constituent found in the several plant products which we call *resins.* These bodies are best defined as plant substances soluble in alcohol, insoluble in water, and dissolving in alkalis to form "resin soaps." Hence they are acid in character. Whether all the resins considered in this chapter will on investigation comply with this definition remains to be seen, and let it be distinctly understood that practically all resins are far more complex than the above definition implies.

Tschirch has attempted a classification of resins as follows:

Resin Esters or Their Saponification Products (Resines):

These esters are combinations of aromatic acids, such as benzoic, cinnamic, and ferulic acids, with resin alcohols (resinoles).

The resin alcohols can be grouped into two classes, according as they do or do not give the tannin reaction, the latter class being called resin-tannols. Among the tannin-free resinols may be mentioned *storesin* in storax; while as examples of resin tannols may be cited *toluresin tannol* in balsam of tolu.

Resinol Acids:

Resin acids, such as abietinic acid in rosin, guaiaconic acid in guaiac, and copaivic acid in copaiba.

Resenes:

Indifferent substances of unknown composition, such as *dracoresene* in dragon's blood.

Aliphato-resins (esters of aliphatic acids), *chromo-resins* (containing coloring matter); *enzymo-resins* (containing enzymes such as laccase); *glucoresins* (esters of resin acids with sugars, such as the glucosides found in Jalap) are known; while the so-called "milk juices" (India rubber, etc.) are now considered as *lacto-resins.*

Resins are sometimes extracted from drugs by means of solvents (example: the resin from phytolacca); sometimes represent practically entire plant exudation (example: mastic); frequently exude from plants combined with volatile oils, then forming the class of drugs called *oleoresins* (example: turpentine, N.F. VI); and often exuding mixed with gummy substances, such an exudation being called a *gum resin* (example: asafetida). Occasionally, the resin which exudes is aromatic by reason of the benzoic and cinnamic acid it contains, the example of such a *balsamic resin* being benzoin (p. 875), while natural oleoresin similarly flavored with benzoic and cinnamic acid is called a *balsam* (example: balsam of Tolu (p. 866). The last two classes of drugs as well as the oleoresins were discussed in the preceding chapter. It is advisable right here again to call attention to the distinction between natural and pharmaceutic oleoresins, already discussed on p. 275.

Neutral principles are plant principles of whose structural chemistry —of whose position in systematic chemistry—we know little or nothing. They are usually bitter and crystalline, are neither basic like alkaloids nor derivatives of glucose, as are the glucosides. That the grouping is purely artificial and temporary is shown by the fact that the most carefully studied neutral principle, santonin, is now known to be a lactone derived from hexahydrodimethyl-naphthalin and will eventually be considered in textbooks among the naphthalin derivatives, even as coumarin, a lactone of oxycinnamic acid, is studied among the derivatives of allylbenzene (p. 818).

RESINS, GUM-RESINS, AND DRUGS CONTAINING NEUTRAL PRINCIPLES

Guaiacum (N.F. VI), or *Guaiac Resin*, is obtained from *Guajacum officinale* and from *Guajacum sanctum*. It contains *guaiaconic acid* (now said to be a mixture), *guaiaretic acid*, $C_{26}H_{24}O_4$, *guaiacinic acid* (or beta-resin), a saponin yielding *guagenin* upon hydrolysis; vanillin, volatile oil, etc.

Tschirch inclines to the belief that these so-called "acids" are resin alcohols. The alcoholic solution is characterized by turning blue in the presence of oxidizing agents, such as ferric chloride or even the enzymes of acacia (p. 708).

By reason of this property filter paper steeped in tincture of guaiac is used as a test paper for ozone and for blood, the hematin of the latter as the oxidizing agent.

Medical Properties.—Alterative in syphilis and rheumatism. The *tincture* (p. 253), and the *ammoniated tincture* (p. 253) are recognized by the National Formulary.

Dose.—Of drug, 1 Gm. (15 grains).

Guaiacum Lignum (U.S.P. 1890; N.F. IV), or *Guaiac Wood*, the wood from which the above resin is derived. It owes its properties almost entirely to the resin, although it is said to also contain a saponin.

Mastiche (N.F. VI), or *Mastic*, is a concrete resinous exudation from *Pistacia lentiscus* Linné (Fam. *Anacardiaceæ*).

Mastic contains *masticic acids* (two isomeres, $C_{23}H_{36}O_4$); *masticonic acids* (two isomeres, $C_{32}H_{48}O_4$); *masticolic acid*, $C_{23}H_{36}O_4$; *mastico-resenes* (the "beta" variety formerly called *masticin*); volatile oil 2 per cent. It is used as a carminative (dose, 30 grains) and is a constituent of *pills of aloes and mastic*, N.F.

Burgundy pitch is no longer official. It is a resin prepared from a species of fir, and is used in medicine exclusively for the preparation of plasters.

Resin of copaiba (U.S.P. 1890), while considered as a pharmaceutic on page 306, is worthy of a few lines devoted to its chemistry. It is the residue left on distillation of official copaiba, and consists largely of a solid acid—in this case, *copaivic acid*. As mentioned on page 296, this acid combines with moist magnesium oxide to form a salt, and to this action is due the solidification of oleoresin in making mass of copaiba.

RESINA—Rosin

(Colophony)

Rosin is a solid resin obtained from *Pinus palustris* Miller and from other species of *Pinus* (Fam. *Pinaceæ*).

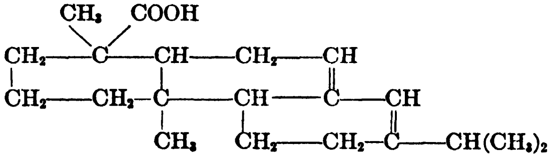
Summarized Description.

Sharply angular, translucent, amber-colored fragments; brittle at ordinary temperatures; terebinthinate odor and taste; freely soluble in alcohol, ether, benzene, glacial acetic acid, fixed and volatile oils and in diluted alkaline hydroxide solutions; sp. gr. 1.07 to 1.09. For details, see U.S.P., p. 319.

Acid Number.—No less than 150. Details in U.S.P., p. 319.

Constituents.—Alpha-resin acid, 31 per cent; beta-resin acid, 31 per cent; gamma-resin acid, 19 per cent; resene, 10 per cent; volatile oils, 0.5 per cent.

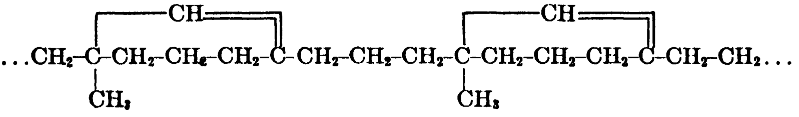
The resin acids mentioned above are combined in the substance called *abietic acid* or *abietic anhydride*; the formula according to Vocke being



Remarks.—As already mentioned (p. 862), rosin is the resinous constituent of the natural oleoresin, *turpentine*, and is obtained by distilling the volatile oil—the so-called "spirit of turpentine"—therefrom.

Medical Properties.—Mild irritant. Used chiefly externally as constituent of plasters, cerates, and ointments. Official preparation: *Rosin cerate* (p. 361).

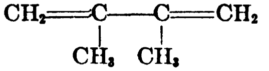
Elastica (U.S.P. VIII), or *Rubber*, is the prepared milk-juice of several species of *Hevea*. It is a polymerized isoprene and its formula is supposed to be:



This configuration is incomplete. Staudinger believes that the molecular weight of rubber is as high as 64,000, which would indicate the presence of almost 1000 C_5H_8 groups.

During the past thirty years, a type of rubber has been produced commercially in Mexico and southwestern United States from the guayule shrub, *Parthenium argentatum*.

Since rubber consists largely of isoprene, the condensation (polymerization) of this hydrocarbon should produce rubber. This condensation has now been accomplished, though who was the first to obtain genuine rubber by this method is a matter of controversy. The synthesis has not as yet become financially feasible, although work to prepare cheap isoprene from dimethyl-butadiene



$$CH_2{=}C(CH_3){-}C(CH_3){=}CH_2$$

which in turn is made from acetone, which is made cheaply from acetylene, produced from calcium carbide, indicates possibility of synthesis at a reasonable price. However, systematic cultivation of rubber plants still forms the cheapest source of supply.

Brazilian rubber from the earliest days has been prepared by submitting the fresh juice to the action of smoke made by burning fatty fuel—like palm fruit—which is allowed to smoulder with but slight access of air. The milk juice is held over the smoke on a wooden paddle, which has been dipped into a bucket containing the juice, and by deft manipulation the liquid juice is prevented from dripping from the paddle until it solidifies. The paddle containing the dried rubber is again dipped into the fresh juice, and the paddle once more rotated over the smoke until that layer has solidified, and this process continued until the paddle holds a large mass of rubber.

Work carried out during the last decade in rubber plantations of Sumatra has developed a spraying process. The milk juice is transported from Sumatra to this country in tanks and upon arrival is dried by throwing it upon a rapidly revolving disk at the top of a tower when it is sprayed into a heated current of air or inert gas.

Rubber is a plastic elastic mass which when heated to above 125° C. becomes a sticky mass, and the products made from it should, therefore, be kept from undue heat. Rubber goods can best be preserved by keeping immersed in water.

Rubber is made more durable by the process of vulcanization. In making soft rubber it is kneaded with 10 per cent sulfur (or a metallic sulfide) at a temperature of 120° to 136° C., while in making hard rubber the crude rubber is heated with 30 to 35 per cent sulfur to 140° to 142° C., and further hardened with rosin, chalk, etc.

Rubber used in medicine is the pure native unvulcanized variety. The only medical use of rubber is as a plaster base.

Duprene is a synthetic rubber prepared in the United States on a commercial scale, using the following sequence of procedure: acetylene→monovinylacetylene→chloroprene (2-chloro-1,3-butadiene). This, by cautious polymerization, is converted into rubber.

Gutta-percha is the prepared milk juice of various trees of the genus *Palaquium*. It resembles rubber in many respects, although it is less elastic and does not readily vulcanize. It is used in surgery for preparing splints.

BENZOINUM—Benzoin

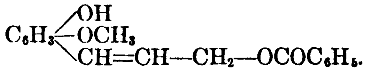
(Benzoin.)

Benzoin is the balsamic resin obtained from *Styrax Benzoin* Dryander, known in commerce as Sumatra Benzoin, or from *Styrax tonkinensis* (Pierre) Craib et Hartwich, or other species of *Styrax*, known in commerce as Siam Benzoin (Fam. *Styraceæ*).

Sumatra Benzoin yields not less than 75 per cent of alcohol-soluble extractive and not more than 1 per cent of acid-insoluble ash. Siam Benzoin contains not more than 1 per cent of foreign organic matter, yields not less than 90 per cent of alcohol-soluble extractive and not more than 0.5 per cent of acid-insoluble ash.

Constituents.—Resin, benzoic acid, cinnamic acid, vanillin, etc.

The resin of Sumatra benzoin consists chiefly of *benzoresinol*, $C_{16}H_{26}O_2$, *sumaresinol*, $C_{20}H_{48}O_{48}$, and *benzoresinotannol*, $C_{18}H_{20}O_4$. That of the Siam variety contains *benzoresinol*, *siaresinol*, *siaresinotannol*, $C_{12}H_{14}O_3$, and *lubanol benzoate*,



$$C_6H_3\begin{cases}OH\\OCH_3\\CH{=}CH{-}CH_2{-}OCOC_6H_5.\end{cases}$$

Remarks.—Benzoin would be considered a balsam, save that the quantity of volatile oil it contains is so small that its base can hardly be considered as an oleoresin. Accordingly, the Pharmacopœia calls it "a balsamic resin."

Benzoin is interesting as the original source of benzoic acid, which thus received its name.

The Pharmacopœia permits the use of two commercial varieties of benzoin—Siam and Sumatra. Of these, the former possesses a delightful odor of vanilla, and is used by perfumers in preference to the less aromatic Sumatra variety. Medicinally, the two are about equal.

Recently organic chemists have used the name "benzoin" for a series of benzylphenyl ketones. This is an unwarranted misuse of a historic name.

Medical Properties.—Expectorant. Used chiefly externally as an antiseptic and vulnerary. The *tincture* (p. 245) and the *compound tincture* (p. 245) are official. It is also used in making *benzoinated lard* (p. 738).

Dose.—1 Gm. (15 grains).

Chicle is the milk juice of *Achras Sapota*, a tree growing in Central America. It consists of the alcohols α- and β-amyrin and lupeol, combined as esters with acetic, capronic, cinnamic and benzoic acids. Its use in chewing gum is well known.

GUM-RESINS

Gum-resins are plant exudations consisting of gum and resin. We have already learned what a gum (p. 705) is, and wherein a resin (p. 872) differs from a gum, the pharmaceutic difference being one of solubility, resins dissolving in alcohols and being insoluble in water, while gums dissolve in water and not in alcohol. Again, resins are terpene derivatives, while gums are dissociation products of cellulose.

The gum of a gum resin will not dissolve in alcohol; the resin will; and since the resin is the active constituent, tinctures of such drugs are made by maceration in 95 per cent alcohol and filtration of the resinous solution from the undissolved gum. In water, the gum will dissolve and the resin will not, but by rubbing such a drug with water the mucilage formed by the dissolved gum emulsifies the resin—also the volatile oil, if any be present—making a milky mixture. Such a mixture is formed when asafetida is rubbed with water, and since the preparation is clearly a form of emulsion, it is so termed by the Pharmacopœia. Up to the revision of 1890 they were grouped with the mixtures of the Pharmacopœia. Two gum resins are now official, asafetida and myrrh, and of these, the first is a representative of the Umbelliferæ—that family of plants to which belong anise, fennel, coriander, and caraway. The second belongs to the Burseraceæ Family.

ASAFŒTIDA—Asafetida

(Asafœt.—Gum Asafetida)

Asafetida is the gum-resin obtained by incising the living rhizomes and roots of *Ferula Assa-fœtida* Linné and *Ferula fœtida* (Bunge) Regel and of other species of *Ferula* (Fam. *Umbelliferæ*).

Asafetida yields not less than 50 per cent of alcohol-soluble extractive, and not more than 15 per cent of acid-insoluble ash.

For *tests for identity* and for *impurities* (foreign resins, galbanum, ammoniac), see U.S.P., p. 75.

Outline of Assay.—The drug is digested with boiling alcohol in a Soxhlet or other extraction apparatus for three hours; the mixture is filtered through counterpoised filters; the insoluble residue is washed with boiling alcohol and is then weighed. Weight should be not more than 50 per cent of the original asafetida taken. For details, see U.S.P., p. 75.

Constituents.—Resin, 50 to 69 per cent; gum, 25 to 31 per cent; bassorin; volatile oil.

The resin consists of the ferulaic acid (p. 819), ester of *asaresinotannol*, $C_{24}H_{33}O_4OH$; while the oil is a mixture of sulfides, $C_7H_{14}S_2$, $C_{11}H_{20}S_2$, $C_8H_{16}S_2$, and $C_{10}H_{18}S_2$, with terpenes. Powdered asafetida is practically without value, as the amount of heat necessary to dry it drives off nearly all of the volatile oil.

Medical Properties.—Antispasmodic (in hysteria), carminative. The *emulsion* U.S.P. XI (p. 286), *pills* N.F. VI (p. 340), and *tincture* N.F. VI (p. 252) are official, and the tincture is an ingredient of the popular colic cure, *Dewee's Carminative* (mixture of magnesia, asafetida and opium, N.F. V). As this mixture contains opium, its use is not advisable, and some physicians specify the preparation "without opium," in which case it is made exactly as per the Formulary, save that the tincture of opium is omitted.

Dose.—Of drug, 400 mg. (6 grains).

Cambogia (U.S.P. X; N.F. VI), or *Gamboge*, is the gum resin obtained from *Garcinia Hanburyi*. It contains 16 per cent of gum and 77 per cent of resin. The resin consists of three *garcinolic acids*. The alpha and gamma varieties have the formula $C_{22}H_{27}O_4COOH$; while the beta acid is $C_{24}H_{34}O_4COOH$. The resin on fusion yields phloroglucin and fatty acids. *Medical Properties.*—Hydragogue cathartic. Always in combination, since it is very drastic. An ingredient of *compound cathartic pills* (N.F. VI) (p. 340). *Dose.*—125 mg. (2 grains).

MYRRHA—Myrrh

(Myrrh.—Gum Myrrh)

Myrrh is a gum resin obtained from *Commiphora Abyssinica* (Berg) Engler or from other species of *Commiphora* (Fam. *Burseraceæ*).

Myrrh yields not less than 30 per cent of alcohol-soluble extractive and not more than 5 per cent of acid-insoluble ash.

Constituents.—Gum, 60 per cent; resin, 30 per cent; volatile oil, 6 to 7 per cent.

The resin consists of α and β *Myrrols*, $C_{17}H_{24}O_5$ and $C_{19}H_{28}O_4$ respectively; of α and β *Myrrholols*, $C_{30}H_{44}O_{14}$ and $C_{29}H_{36}O_{10}$ respectively; and of a resene $C_{29}H_{40}O_4$. The gum hydrolyses to galactose, arabinose and xylose. The volatile oil appears to be closely related to the resene. Bolton claims that the antiseptic activity of myrrh is due to *burserazin*, $C_{20}H_{28}O_8$.

Incompatibilities (*of tincture*).—See prescription No. 34 in Chapter LIX.

Medical Properties.—Carminative. The official *tincture* (p. 249) is a useful addition to mouth washes.

Dose.—500 mg. (8 grains).

Ammoniac, the gum resin from *Dorema Ammoniacum,* was dropped in the eighth pharmacopœial revision. It contains volatile oil, resin (chiefly *ammoresinol,* $C_{16}H_{17}(OH)(OCH_3)_2$), and gums, including bassorin. It is a stimulant, and given in doses of 15 grains.

Galbanum, U.S.P. 1880, is the gum resin from *Ferula galbaniflua.* It contains volatile oil, gum, and a resin containing umbelliferon.

RESIN DRUGS

The following drugs are said to owe their activity to resinous matter not associated with volatile oil.

Phytolacca (N.F. VI), or *Poke Root,* is the dried root of *Phytolacca americana* Linné (Fam. *Phytolaccaceæ*), collected in autumn. It contains resin, tannin, a glucoside, trace of volatile oil, trace of alkaloid, and a volatile acid, and is used as an alterative (in rheumatism); in large doses it is emetic. Dose as alterative is 1½ grains, as emetic is 15 grains.

Poke Berries, the fruit of *Phytolacca decandra,* were formerly official. They are emetic and cathartic, and of supposed value in reducing superfluous flesh. *Dose.*—15 grains.

Gossypii Radicis Cortex (N.F. VI), is the dried bark of the root of *Gossypium herbaceum* Linné, or of other cultivated species of *Gossypium* (Fam. *Malvaceæ*).

It contains a volatile oil, acids (dihydroxy-benzoic, and salicylic), phenols, betaine, fat, and sugar. It is used as an emmenagogue, and should not be sold indiscriminately, being frequently used to produce abortion. It is used as an emmenagogue and ecbolic, in 30-grain doses.

Rhus Toxicodendron, U.S.P. 1890, are the leaves of a number of species of *Rhus,* there being 19 species of this genus which possess the peculiarly poisonous properties of this drug. "Rhus Tox" is largely employed by homeopaths in attenuated doses, but has fallen into disuse by regular medical practitioners. Our sole interest in the plants of this genus is because they yield *poison oak* (*R. toxicodendron*) and *poison ivy* (*R. radicans*), producing the disagreeable and painful skin eruptions known far too well by too many.

The cause of this toxic action is still a matter of controversy, McNair stating that it is a phenol, which he called *lobinol.* Older writers ascribed the poisonous effect to an oily substance, *toxicodendrol.*

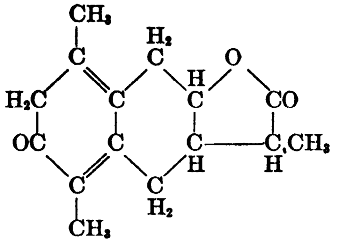
The only remedies for ivy poisoning are external applications (salts such as sodium bicarbonate) or alcoholic preparations (sweet spirit of nitre or tincture of grindelia). McNair and also Stoneback recommend use of a wash made from solution of ferric chloride (5 per cent), glycerin (42.5 per cent) and water (42.5 per cent). There are now on the market alcoholic and oleaginous solutions of poison ivy extract for use by intramuscular injection for ivy poison.

NEUTRAL PRINCIPLES AND DRUGS CONTAINING SAME

SANTONINUM—Santonin

(Santonin.)

$C_{15}H_{18}O_3$



Molecular weight, 246.14

The inner anhydride of santoninic acid.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, shining flattened rhombic prisms or crystalline powder; first tasteless, then bitter; becomes yellow on exposure to light; discolored samples recrystallize white from alcohol; soluble in about 5300 parts of water, and in about 34 parts of alcohol; also soluble in chloroform and ether; solutions are levorotatory; melts between 169° and 171° C. For details, see U.S.P., p. 324.

For *tests for identity* and for *impurities* (carbonizable substances, alkaloids), see U.S.P., p. 324.

Extraction.—The drug is mixed with slaked lime and after drying and grinding, the alkaline mixture is percolated with warm alcohol or with hot water. The alcohol is distilled from the percolate and to the residue hydrochloric acid is added. After the acidulated liquid is allowed to stand five days the crystals of santonin are collected and purified.

Composition.—The graphic formula given above is that suggested by Cannizzaro. Chemo and Haworth (p. 887) give a slightly different configuration. Each of these formulæ represents a derivative of hexahydronaphthalene.

Remarks.—The change to yellow on exposure to light is said to be due to its conversion into *photosantonic acid.* According to Piutti, the two bodies are isomeres, the change being due to a shift of the double bonds. The change emphasizes the importance of keeping santonin and its preparations in a dark place.

Medical Properties.—Anthelmintic; should be used with caution, since it has been known to produce blindness. Usually administered in the form of the *troches* or *tablets.*

Dose.—60 mg. (1 grain).

Santonica (U.S.P. VIII), or *Levant Wormseed,* is the dried, unexpanded flower-heads of *Artemisia pauciflora* (Ledebour) Weber (Fam. *Compositæ*). Santonica contains santonin (2 per cent), and volatile oil (2 per cent). The volatile oil consists of *cineol* (p. 836) and *cajuputene* (or *cinene*).

Santonica is one of the two drugs called "wormseeds," and neither are seeds. The other wormseed, chenopodium, is a fruit, while santonica is a tiny cluster of unopened flowers. The two are readily distinguished by rubbing the specimen between the thumb and forefinger. If chenopodium, a little chaff rubs off, leaving a minute black seed; if santonica, the entire specimen rubs into dry, chaffy scales. Santonica is important as the source of santonin.

It is rarely used as a drug, but when so employed as an anthelmintic, its dose is 30 grains.

Elaterinum (U.S.P. X), or *Elaterin,* is a substance obtained from the juice of the fruit of *Ecballium Elaterium.* Power and Moore state that the commercial elaterin is a mixture. One of the constituents, α-elaterin, $C_{28}H_{37}O_7$, is levogyrate; while the physiologically active constituent, β-elaterin, $C_{28}H_{38}O_7$, is dextrogyrate. These elaterins are neutral principles obtained from elaterium. This, in turn, is a constituent of the juice of the squirting cucumber, *Ecballium Elaterium,* which is a plant belonging to the gourd family. The pronunciation of the two words is different, the accent in the official name being on the second syllable (e-*lat*-er-in), while in the other word it is on the third syllable (el-a-*ter*-i-um). Elaterin is a hydragogue cathartic.

Dose.—3 mg. (1/20 grain).

Picrotoxin, $C_{15}H_{16}O_6$, which was formerly official, is the active principle of *fishberries* (*Animirta Cocculus*). It is now supposed to be a mixture of picrotoxinin, $C_{14}H_{16}O_6$, and picrotin, $C_{15}H_{18}O_6$. It is a dangerous poison, and is used chiefly for killing body vermin. Its dose is 1 mg. (1/64 grain).

Cocculus (N.F. VI) are the *fishberries* just mentioned. Besides picrotoxin, they contain menispermine, picrotoxic acid and cocculin. They are used in the form of an infusion or tincture for destroying head lice.

Taraxacum (N.F. VI), or *Dandelion*, represents the rhizome and roots of *Leontodon Taraxacum.* It contains brown, amorphous, bitter principle; resinous matter; inulin; choline; levulose; acids (hydroxy-phenylacetic, etc.); trace of volatile oil.

The resin is a combination of phytosterols (taraxasterol, cluytianol, etc.) with fatty acids (palmitic, melissic, oleic, etc.). Taraxacin and taraxacerin of older writers are mixtures.

The synonym, dandelion, comes from the French "dent de lion," the lion's tooth, so termed after the jagged edges of its leaves. It is a good remedy in liver trouble. Look out for prescriptions containing fluidextract of taraxacum and nitrohydrochloric acid. Both are valuable hepatic stimulants, but when mixed they are apt to explode (p. 456).

The drug should be collected in the autumn. This is because the young root collected in the spring contains little or no bitter principle and much sugar. During the summer the latter is converted into the inulin found in the official drug.

Dandelion is a hepatic stimulant and digestive and is given in 4-Gm. doses. The *extract* and the *fluidextract* are recognized by the National Formulary.

Calumba (U.S.P. X; N.F. VI), or *Columbo*, is the dried root of *Jateorrhiza palmatum.* It contains *columbin*; *columbic acid*; three alkaloids, *columbamarine*, *jateorrhizine*, and *palmitine*; starch; no tannin. Columbin is a bitter principle, to which several formulas have been assigned by different investigators. Frey says it is $C_{27}H_{28}O_9$, and is a lactone. On treatment with alkali it yields columbic acid, $C_{28}H_{32}O_{10}$. The three alkaloids resemble berberine and give the drug its yellow color. Calumba is a simple bitter. The *tincture* (p. 252) and the *fluidextract* (p. 270) are recognized by the Formulary. *Dose.*—1 Gm. (15 grains).

PODOPHYLLUM—Podophyllum

(Podoph.—Mandrake, May Apple)

Podophyllum consists of the dried rhizome and roots of *Podophyllum peltatum* Linné (Fam. *Berberidaceæ*).

Podophyllum yields not less than 4 per cent of the resin of podophyllum, and contains not more than 3 per cent of foreign organic matter.

Constituents.—*Picropodophyllin; picropodophyllinic acid; podophyllinic acid*; green oil; resin; starch, etc.

Picropodophyllin is a bitter principle, $C_{23}H_{24}O_9 2H_2O$, while picropodophyllinic acid has the formula $C_2\,H_{24}O_9$, and is physiologically inactive. The two combine to form *podophyllotoxin.*

Podophyllum is the rhizome of an American plant commonly called *may apple*, or *mandrake.* It yields that important purgative, podophyllin, which is official under the name of *resin of podophyllum* (p. 305), since it is not a definite chemical, but a mixture of the active principles of the drug, cited above, associated with resin. Too great stress cannot be laid on the difference between *podophyllum*—the rhizome—and *podophyllin*—the trade name for resin.

Medical Properties.—Hydragogue cathartic. Usually administered with other purgatives. The *resin* (cited above) is official.

Dose.—No dose is given in the present Pharmacopœia. In the eighth edition it was stated as 500 mg. (7½ grains).

Quassia (U.S.P. X; N.F. VI), or *Bitter Wood*, is the wood of *Picrasma excelsa* and of *Quassia amara.* The former plant yields Jamaica quassia, while the latter is the source of Surinam quassia. Both types contain *quassin*, *picrasmin*, mucilage, resin, etc.

Quassia is the wood of the two different trees, and its bitterness is well known. Its use in the form of drinking cups was quite popular some years since, but is no longer in vogue. Quassia is used as a bitter tonic. *Dose.*—500 mg. (8 grains).

SANTALUM RUBRUM—Red Saunders

(Santal. Rub.)

Red Saunders is the heart wood of *Pterocarpus santalinus* Linné filius (Fam. *Leguminosæ*).

Constituents.—*Santalin* (or *santalic acid*), $C_{15}H_{14}O_5$, a red coloring principle.

Medical Properties.—Used entirely as coloring agent, and employed for this purpose in *compound tincture of lavender* (p. 249).

Apocynum (N.F. VI), or *Canadian Hemp*, is the dried rhizome of *Apocynum cannabinum.* It contains *apocynin* or *acetovanillin*, $C_9H_{10}O_3$; *cynotoxin*, $C_{20}H_{28}O_6$ (a powerful heart stimulant, resembling Kiliani's digitic acid); *cymarin*; resin, and tannin. It is used as a cardiac tonic and diuretic in 3-grain doses. It is by no means innocuous and should be given only under the watchful eye of a careful physician.

Euonymus (U.S.P. VIII; N.F. V), or *Wahoo Bark*, is the dried bark of the root of *Euonymus atropurpureus.* It contains euonymol, $C_{21}H_{30}O_4$, resinous matter; volatile oil (trace), dulcit, sugar, tannin, etc. The resin consists of phytosterols (euonysterol, citrullol, etc.) and fatty acids (palmitic, cerotic, oleic, etc.). No glucosides are present. Euonymus is used as a laxative and diuretic in 8-grain doses.

Brayera (U.S.P. VIII; N.F. V), or *Cusso* or *Kousso*, represents the dried pannicles of the pistillate flowers of *Hagenia abyssinica.* It contains resinous principle, $C_{23}H_{30}O_7$, called *tænin*, or *kosin*; tannin, etc.

Cusso is used as a tenifuge or remover of tapeworm. It is usually administered in the form of an unstrained infusion, it being claimed that the action is largely mechanical. *Dose.*—240 grains.

Castela Nicholsoni (*Bitter Bush* or *Chaparra Amargosa*) is a plant that has enjoyed considerable vogue in southwestern United States as a remedy for dysentery. It contains a bitter principle, *castelamarin*, and a glucoside, *castelin.*

Caulophyllum (U.S.P. 1890; N.F. V), or *Blue Cohosh*, represents the rhizomes and rootlets of *Caulophyllum thalictroides.* It contains saponin, 2 resins, starch, gum and *caulophyllin* (methyl cytisin, $C_{12}H_{16}N_2O$). It is used as a demulcent, diuretic and emmenagogue in 0.5-Gm. doses.

Lactucarium (U.S.P. IX) is the dried milk juice of *Lactuca virosa*, which is the wild lettuce, a plant closely allied to our garden lettuce. The wild variety, when plucked, exudes a milk juice. Such juice on drying yields the official drug, which is a useful sedative. Each lettuce plant naturally yields a comparatively small amount of juice, and when it is remembered that the dried juice must be scraped from each cut plant, the high price of lactucarium is explained.

It contains *lactucin*, *lactucerin*, *lactucic acid*, *lactucopicrin*, acetate of *lactucerol*, gum, resin, caoutchouc, or waxy substance.

The rubbery or waxy constituent of lactucarium can be extracted with benzin, which solvent does not remove the active constituents. Hence the use of benzin in preparing the formerly official *tincture* (p. 253).

Medical Properties.—Mildly narcotic. Useful in hacking coughs.

Dose.—1 Gm. (15 grains).

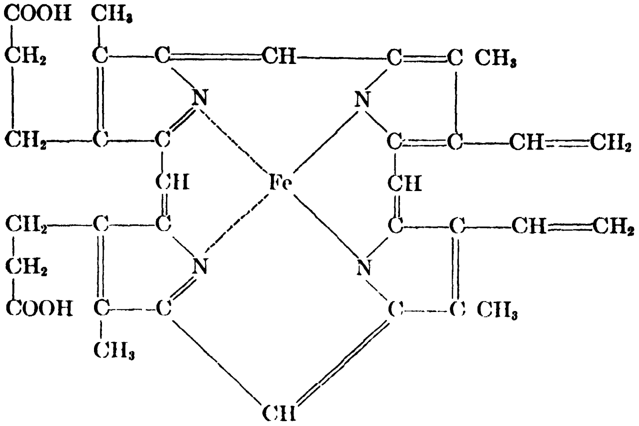
PLANT AND ANIMAL COLORS

The natural pigments found in vegetable and in animal tissue can well be discussed in this chapter, since, like neutral principles, they represent complex compounds, the structure of which are in most cases not sufficiently understood to permit their proper classification. Among these substances we find:

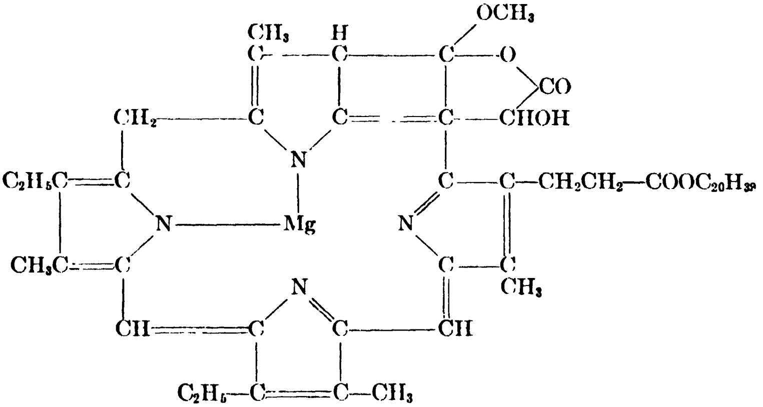
Chlorophyll and Other Leaf Pigments.—The green color of leaves is now known to consist of four pigments: chlorophyll "a," $C_{55}H_{72}O_5N_4Mg$; chlorophyll "b," $C_{55}H_{70}O_6N_4Mg$; carotin, $C_{40}H_{56}$; and xanthophyll, $C_{40}H_{56}O_2$. The first two are green, while the last two are yellow. No less than 36 intermediate products between the two chlorophylls "a" and "b" have been prepared and analyzed by Willstätter and his pupils. These—

phæophytins, phytorhodins, porphyrins, ætiophyllin, etc.—have blue, red and yellow tints.

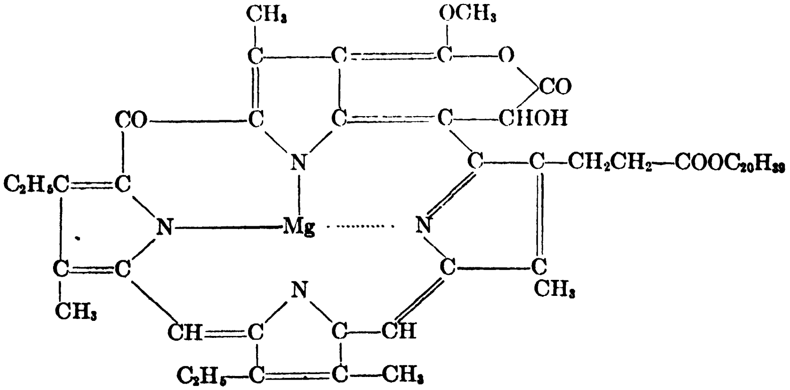
According to Küster and to Fischer the structural formula of hemin, the blood pigment, is:



According to Conant and his coworkers the structural formula of chlorophyll A is



while these investigators represent chlorophyll B as follows:



There is a striking resemblance between the structural formulæ of the chlorophylls, the porphorins and hemin. Fischer expresses these relationships schematically as follows:

$$\text{Hemin} \rightleftarrows \text{Pyrroporphorin} \rightleftarrows \text{Chlorophyll.}$$

Fischer's recent formula (1934) for chlorophyll "a" differs from the Conant formula given above; hence the structure of this plant pigment cannot be said to be definitely settled.

Floral Colors, or *Anthocyans,* are glycosides that hydrolyze to sugar and *antrocyanidins.* Willstätter has isolated three of the latter, *cyanudin, pelagonidin, delphinidin,* and has shown that they are complex naphthalin derivatives. Willstätter obtained cyanidin chloride, $C_{15}H_{11}O_6Cl$ by the reduction of quercetin (p. 883) while Robinson and his coworkers have synthesized no less than four isomeric glucosides of pelargonidine chloride, $C_{15}H_{11}O_5Cl$.

Hematin, the blood pigment, is described on page 952, while the structure of its halogen compound *hemin* is given above.

Flavone, $C_{14}H_{10}O_2$, is the basic principle of a number of plant colors. Among the flavone derivatives may be cited *quercetin* from oak bark, *hesperetin,* the hydrolysis product of hesperidin (p. 714), lapachol, or methobutanyloxynaphthaquinone from *Nectandra rhodiœi* and from *Tecoma chrysotrica,* and chrysoeriol, from yerba santa (p. 858).

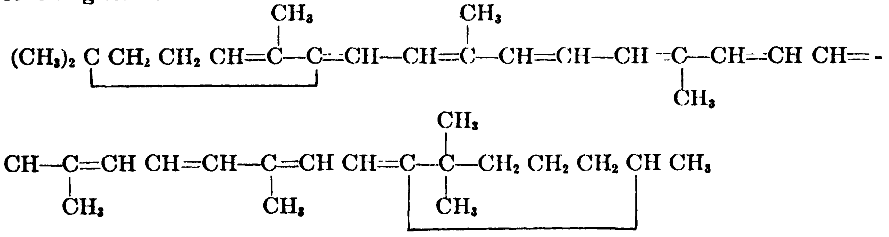
Hæmatoxylin, $C_{16}H_{14}O_6$, and **Hæmatin,** $C_{16}H_{12}O_6$, are coloring principles found in logwood (p. 811). Note that the hæmatin of logwood is not the same as the hematin of the blood.

Curcumin, $C_{21}H_{20}O_6$, is the coloring matter found in turmeric, which makes this substance of value in testing for boric acid (p. 436).

Azulene, $C_{15}H_{18}$, is the blue coloring matter found in oil of matricaria (p. 861).

Bilirubin, $C_{33}H_{36}N_4O_6$, is a bile pigment with structure similar to hemin of the blood.

Carotin or **carotene,** $C_{40}H_{56}$, is a hydrocarbon which according to Karrer has the following structure:



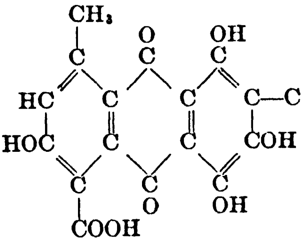
$$(CH_3)_2\,C\,CH_2\,CH_2\,CH{=}\overset{CH_3}{C}{-}C{=}CH{-}CH{=}\overset{CH_3}{C}{-}CH{=}CH{-}CH{=}\underset{CH_3}{C}{-}CH{=}CH\,CH{=}-$$

$$CH{-}\underset{CH_3}{C}{=}CH\,CH{=}CH{-}\underset{CH_3}{C}{=}CH\,CH{=}C{-}\overset{CH_3}{\underset{CH_3}{C}}{-}CH_2\,CH_2\,CH_2\,CH\,CH_3$$

It is the color of carrots and of many oils and is a constituent of crude chlorophyll (p. 880). Recent investigations indicate its close relationship to vitamin A (p. 957).

Xanthophyll, another yellow plant pigment and a constituent of crude chlorophyll, is dihydroxycarotene, $C_{40}H_{56}O_2$.

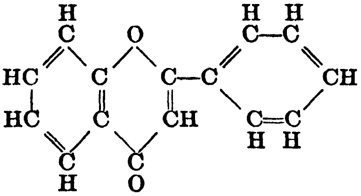
Carminic Acid, $C_{22}H_{20}O_{13}$, the color of cochineal (p. 960) is presumably



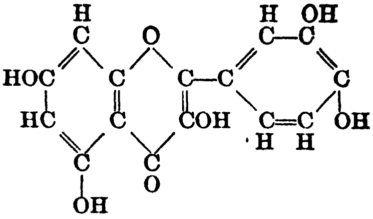
Orcein is a red coloring matter obtained from lichen colors such as *orchil* and *cudbear.* These represent the lichens such as *Rocella tinctoria* and *Pertusaria dealbata* treated in certain ways in order to develop the desired color. The active principles of these colored lichens are said to be *lecanoric acid,* $C_{16}H_{14}O_7$, *orsellic acid,* $C_8H_8O_4$, and *orcin,* $C_7H_8O_2$. The latter upon treatment with ammonia yields orcein, $C_{28}H_{24}N_2O_7$, which becomes a brilliant red upon treatment with alkalis. Orcin is methylresorcinol $C_6H_3{}^{CH_3}_{(OH)_2}$.

Below are given the graphic formulæ assigned to some of the substances just described:

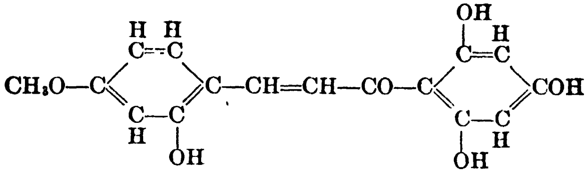
Flavone



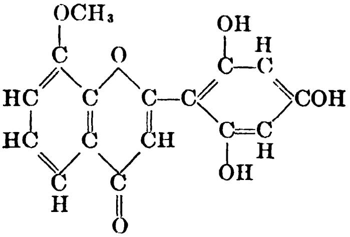
Quercetin



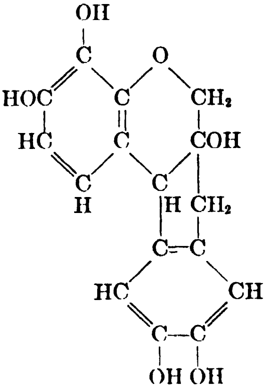
Hesperetin



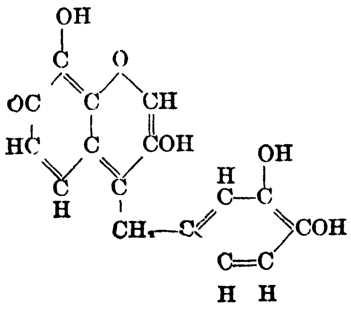
Chrysoeriol



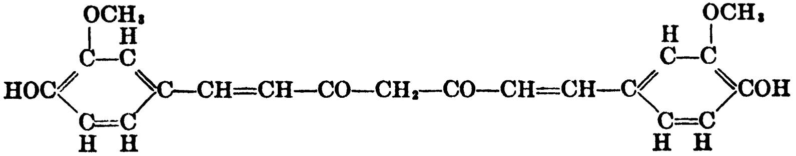
Hæmatoxylin



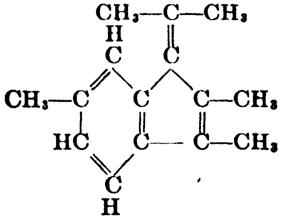
Hæmatin



Curcumin



Azulene



BIBLIOGRAPHY

Resins.—(General) Frankforter, Science, 36, 1912, 257; Tschirch, Ph. Jl., 102, 1919, 219; McNair, C.A., 24, 1930, 4078.

Guaiacum.—(Constituents) Doebner and Lücker, Arch. d. Pharm., 234, 1896, 590; Richter, Arch. d. Pharm., 244, 1906, 90; Schroeter, Lichtenstadt and Irinen, Jl. Ch. Soc. Abs., 116, 1919, 84; Haworth and Mavrin, C.A., 26, 1932, 4044. (Incompatibility) Krantz and Carr, Jl. A.Ph.A., 18, 1929, 1153.

Mastic.—(Production) Lloyd, A.J.P., 89, 1917, 1. (Constituents) Tschirch and Reutter, Arch. d. Pharm., 242, 1904, 104; Anon., Schimmel's Rep., April, 1893, 64.

Burgundy Pitch.—Morel, Ph. Jl., [3], 8, 1877, 342.

Resin of Copaiba.—(Constituents) Strauss, A., 148, 1868, 148.

Rosin.—(Constituents) Kremers and Mead, A.Ph.A., 41, 1893, 198; Mach, A.Ph.A., 42, 1894, 1075; Tschirch and Koritschoner, Arch. d. Pharm., 240, 1902, 1584; Tschirch and Binder, *ibid.*, 252, 1914, 547; Reutter, Schw. Ap. Ztg., 51, 1913, 245 and 247; Pooth, C.A., 9, 1914, 2644; Cohn, Ph. Week., 54, 1917, 767; Knecht and Hibbard, Jl. ph. ch., 20, 1919, 324; Johansson, Jl. Soc. Ch. Ind., 39, 1920, 198A; Aschan, C.A., 15, 1921, 3095; 18, 1924, 2151 and 24, 1930, 371; Brün, *ibid.*, 15, 1921, 1298; Stock, *ibid.*, 16, 1922, 504; Madinaveitia, *ibid.*, 17, 1923, 288; Dupont and Uzac, *ibid.*, 18, 1924, 2009. Levy and co-workers, C.A., 7, 1913, 2388; C.A., 20, 1926, 3012; C.A., 22, 1928, 87; C.A., 26, 1932, 470; Knecht and Hibbert, Jl. Soc. Ch. Ind., 44, 1925, 931B; Shaw and Sebrell, Jl. Ind. Eng. Ch., 18, 1926, 612; Dupont and co-workers, C.A., 22, 1928, 423; Fonrobert, C.A., 24, 1930, 1386; Ruzicka and co-workers, C.A., 25, 1931, 3657; Berger, C.A., 26, 1932, 3800; Vocke, C.A., 26, 1932, 5952.

Rubber.—(History) Geer, Jl. Ind. Eng. Ch., 17, 1925, 1024; Porritt, Jl. Soc. Ch. Ind., 45, 1926, 74; Schidrowitz, Jl. Ind. Eng. Ch., 18, 1926, 1147; Slosson, *ibid.*, 18, 1926, 1104; Luft, Jl. Soc. Ch. Ind., 47, 1928, 1129; Speter, C.A., 23, 1929, 4373. (Collection) Coblentz, Pharm. Era, 39, 1908, 488; Labroy and Cayla, C.A., 8, 1914, 2496; Hopkinson, Jl. Soc. Ch. Ind., 43, 1924, B104; King, also Witt, C.A., 10, 1916, 704; Heim and Marquis, C.A., 10, 1916, 399; Van Rossem, Jl. Soc. Ch. Ind., 44, 1925, 33T; Davy, *ibid.*, 44, 1925, 515T. (Chemistry and synthesis) Harries, Ch. Zt., 36, 1912, 654 and A., 406, 1914, 173; Pond, Jl. Am. Ch. Soc., 36, 1914, 165; Anon., Jl. Ind. Eng. Ch., 9, 1917, 984; Anon., Yearbook A.Ph.A., 1918; Schidrowitz, Ch. Age, 4, 1921, 298; Olivier, C.A., 16, 1922, 1237; Kirchhof, Jl. Soc. Ch. Ind., 42, 1923, 23A; Boswell and co-workers, *ibid.*, 42, 923, 63A; Fisher, Jl. Ind. Eng. Ch., 16, 1923, 627; Sturmer, A.J.P., 96, 1924, 721; Staudinger and co-workers, Jl. Soc. Ch. Ind., 43, 1924, 756B; C.A., 20, 1926, 2091 and 3588; Weil, Jl. Ind. Eng. Ch., 18, 1926, 1174; Dugué, C.A., 22, 1928, 2682; Midgley and Henne, Jl. Am. Ch. Soc., 51, 1929, 1215 and 1294. (Vulcanizing) Anon., Ch. and Dr., 85, 1914, 377; Bary, C.A., 23, 1929, 546; Boggs and Black, Jl. Ind. Eng. Ch., 22, 1930, 748. (Accelerators) Geer and Bedford, Jl. Ind. Eng. Ch., 17, 1925, 393. (Preservation) Anon., C.A., 7, 1913, 272. (Molecular weight) Ott, Jl. Soc. Ch. Ind., 45, 1926, 681B; Pummerer, *ibid.*, 46, 1927, 788B; Meyer and Mark, C.A., 23, 1929, 1524; Staudinger and co-workers, Jl. Soc. Ch. Ind., 48, 1929, 611B and 49, 1930, 872B; C.A., 24, 1930, 3129; C.A., 25, 1931, 2591, 3518 and 3872; C.A., 26, 1932, 2632.

Duprene.—Anon., Jl. Ind. Eng. Ch., News Ed., 9, 1931, 321; Nieuland and co-workers, Jl. Am. Ch. Soc., 53, 1931, 4197; Carothers and co-workers, *ibid.*, 53, 1931, 4203.

Guayule Rubber.—Spence, Jl. Ind. Eng. Ch., 22, 1930, 384.

Gutta Percha.—Maclagan, A.J.P., 18, 1847, 131.

Benzoin.—(Sources) Reinitzer, Arch. Pharm., 264, 1926, 131 and 368. (Constituents) Lüdy, Arch. d. Pharm., 231, 1893, 43 and 461; Reinitzer, A.Ph.A., 58, 1909, 189; Lieb and Zinke, C.A., 13, 1919, 382; Zinke and Dzrimal, *ibid.*, 15, 1921, 1507; Winterstein and Egli, C.A., 26, 1932, 732.

So-called "Benzoins."—Hopper and Wilson, C.A., 23, 1929, 132; Buck and Ide, Jl. Am. Ch. Soc., 52, 1930, 220 and 53, 1931, 1536; Jenkins and Richardson, *ibid.*, 55, 1933, 1618.

Chicle.—Bosz and Cohan, Arch. d. Pharm., 250, 1912, 52; Stillwell, Jl. Ind. Eng. Ch., 23, 1931, 703.

Asafetida.—(Constituents) Polasek, Arch. d. Pharm., 235, 1897, 125; Semmler, B., 23, 1890, 3530 and 24, 1891, 78; Baumann, C.A., 23, 1929, 5010 and 24, 1930, 4583. (Powdered) Thurston, A.Ph.A., 58, 1910, 101.

Gamboge.—(Collection) Anon., A.Ph.A., 44, 1896, 603. (Constituents) Hlasiwetz and Barth, A., 138, 1866, 61; Lewinthal, through Tschirch's "Die Harze," 1, 1906, 838.

Myrrh.—(Constituents) Bonastre, A.J.P., 5, 1833, 139; Tschirch and Bergmann, Arch. d. Pharm., 243, 1905, 641; Tollens and Hauer, B., 36, 1903, 3312; Bolton, Zt. Elektrochem., 14, 1908, 211; Christensen, C.A., 13, 1919, 889; Bohrisch, Jl. Soc. Ch. Ind., 50, 1931, 823B.

Galbanum.—(History) Conrady, Arch. Pharm., 232, 1894, 98. (Sources) Holmes, Ph. Jl., 51, 1891, 194. (Constituents) Conrady, see above; Semmler and Jones, Ph. Era, 53, 1920, 273.

Ammoniac.—(Etymology) Lippmann, Ch. Zt., 33, 1909, 117. (History) Tschirch and Luz, Arch. Pharm., 233, 1895, 540. (Sources) Holmes, Ph. Jl., 79, 1907, 570. (Constituents) Tschirch and Luz, see above; Moss, Ph. Jl., [3], 3, 1873, 742; Roenisch, C.A., 15, 1921, 2281; Michel, Jl. A.Ph.A., 17, 1928, 1172.

Phytolacca.—(Constituents) Connelly, A.J.P., 15, 1843, 169; Partee, A.J.P., 61, 1889, 123; Jenkins, Jl. A.Ph.A., 18, 1929, 573. (Therapeutics) Holmes, Ph. Jl., 105, 1920, 417 and 450; Coates, *ibid.*, 105, 1920, 454.

Cotton Root Bark.—(Constituents) Wayne, A.J.P., 44, 1872, 289; Shaw, A.J.P., 27, 1855, 419; Power and Browning, Ph. Jl., 93, 1914, 420. (Pharmacology) Eckler C.A., 15, 1921, 270.

Rhus Toxicodendron.—(Sources) Warren, Ph. Jl., 83, 1909, 531 and 562. (Constituents) Warren, see above; Acree and Syme, C.A., 1, 1907, 1426; Post and Gilg, Schw. Wsch. Ch. Ph., 50, 1912, 554; McNair, Jl. Am. Ch. Soc., 38, 1916, 1417; 43, 1921, 159; Acree, *ibid.*, 38, 1916, 1421; Muenscher, C.A., 24, 1930, 5108. (Antidotes) Anon., Ph. Era, 66, 1929, 207; Stoneback, Penna. Pharm., 14, March, 1933, 16. (Histology) Youngken and Slothower, A.J.P., 92, 1920, 695. (Toxicology) Youngken and Slothower, see above; Smith, Yearbook, A.Ph.A., 9, 1920, 235; Schamberg, Jl. A.M.A., 73, 1919, 1213.

Santonin.—(Sources and history) Anon., Pharm. Era, 54, 1921, 101; Viehoever, Jl. Am. Ch. Soc., 45, 1923, 1941; Anon., Jl. Soc. Ch. Ind., 47, 1928, 677. (General) Zwaluwenburg, Ph. Arch., 2, 1899, 1; Merck, A.J.P., 6, 1834, 172. (Extraction) Busch, Jl. prakt. Ch., 35, 1887, 322; Chemnitius, C.A., 24, 1930, 3859. (Structure) Cannizzaro, B., 27, 1894, 530; Piutti, C.A., 8, 1914, 339; Cusmano, C.A., 7, 1913, 2221; Haworth and co-workers, C.A., 24, 1930, 621 and 4046; 25, 1931, 708; Ruzicka and Eichenberger, C.A., 25, 1931, 961; Wedekin and Tettweiler, C.A., 25, 1931, 5173; Banchi and Infante, C.A., 26, 1932, 2745; Greene, Jl. A.Ph.A., 20, 1931, 24. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1155. (Pharmacology) Messner, C.A., 19, 1925, 702; Anon., Schw. Apoth. Zt., 65, 1927, 453. (Properties) Villavecchia, B., 18, 1885, 2859. (Uses) Perry, A.J.P., 29, 1857, 568; Lautenschlaeger, C.A., 16, 1922, 439.

Santonica.—(Constituents) Alms, Arch. d. Pharm., 34, 1830, 319; Kahler, Arch. d. Pharm., 34, 1830, 318; Wallach and Brass, A., 225, 1884, 291 and 314.

Elaterin.—(Composition) Power and Moore, Ph. Jl., 83, 1909, 501; Moore, Jl. Ch. Soc., 97, 1910, 1797; Berg, Bull. Soc. Chim., [4], 7, 1910, 385.

Cocculus Indicus.—(Sources) Richard, A., 14, 1835, 332. (Histology) Wallis, Ph. Jl., 107, 1921, 306. (Constituents) Pelletière and Couerbe, A., 10, 1834, 180; Schmidt, A., 222, 1884, 313 and Arch. Pharm., 122, 1884, 184.

Picrotoxin.—(Structure) Horrmann, B., 45, 1912, 2090; Angelico, C.A., 4, 1910, 2457; 5, 1911, 1092; 6, 1912, 352 and 7, 1913, 1715; Sielisch, A., 391, 1912, 1; Prillwitz, Ph. Jl., 105, 1920, 510.

Taraxacum.—(Constituents) Power and Browning, Jl. Ch. Soc., 101, 1912, 2411.

Apocynum.—(Constituents) Schmiedeberg, A.Ph.A., 31, 1883, 290; Poppenhusen, A.J.P., 60, 1888, 168; Finnemore, Jl. Ch. Soc., 93. 1908, 1513 and Proc. Ch. Soc., 25, 1909, 77; Windaus and Hermans, C.A., 9, 1915, 2378; Howell, Jl. Am. Ch. Soc., 52, 1930, 4077; Searle, C.A., 25, 1931, 4247. (Pharmacology) Dale and Laidlaw, Am. Dr., 56, 1910, 165; Allard, C.A., 7, 1913, 2448; von Noorden, C.A., 10, 1916, 1678; Munch and Krantz, Jl. A.Ph.A., 23, 1934, 988.

Castela Nicholsoni.—(Sources and histology) Zufall, Jl. A.Ph.A., 7, 1918, 166. (Constituents) Putegnat, N.R., 12, 1883, 102; Bosman, Jl. Soc. Ch. Ind., 41, 1922, 607A and C.A., 17, 1923, 1645.

Calumba.—(Constituents) Wittstock, Jl. de. Ph., 17, 1831, 77; Boedeke, A.J.P., 20, 1848, 327; Feist, Arch. d. Pharm., 245, 1907, 586; Frey, A., 351, 1906, 372; Spaeth and Böhm, Jl. Soc. Ch. Ind , 41, 1922, 954A; Spaeth and Duschinsky, Jl Soc. Ch. Ind., 44, 1925, 941B; Feist and Dschu, *ibid.*, 44, 1925, 566B; Awe, C.A., 26, 1932, 2744.

Podophyllum.—(Constituents) Podwyssotzki, Ph. Jl., [3], 12, 1882, 1011; Kürcten, Arch. d. Pharm., 229, 1891, 220. Wallis and Goldberg, Quart. Jl. Ph., 4, 1931, 28; Borsche and Niemann, C.A., 26, 1932, 3509 and 27, 1933, 88.

Quassia.—(Constituents) Winckler, Ch. Cent., 7, 1836, 69; Oliveri and Denardo, Jl. Ch. Soc., 46, 1884, 1192; Massuti, A.J.P., 62, 1890, 338.

Red Saunders.—(Sources) Chatterton, Ch. and Dr., 111, 1929, 309. (Constituents) Pelletière, Ch. Cent., 4, 1833, 246; Meier, A., 72, 1849, 320; Weidel, Arch. d. Pharm., 193, 1870, 159; Franchimont, B., 1879, 14; Cain and May, Proc. 7th Int. Cong. App. Ch., 1909, 4b, 85; Dieterle and Stegemann, Arch. Pharm., 264, 1926, 1.

Euonymus.—(Constituents) Rogerson, Jl. Ch. Soc., 101, 1912, 1040.

Kousso.—(Constituents) Wittstein, Ch. Cent., 11, 1840, 412; Bedal, A.J.P., 64, 1892, 304; Flückiger and Buri, Arch. d. Pharm., 205, 1874, 193; Leichsenring, Arch. d. Pharm., 232, 1894, 50. (Infusion) Pereira, A.J.P., 22, 1850, 319.

Lactucarium.—(History) Podolsky, Dr. Circ., 75, Aug., 1931, 18. (Constituents) Aubergier, Comp. rend., 19, 1840, 923; Walz, A., 32, 1840, 85; Ludwig, A.J.P., 20, 1848, 57; Kromeyer, A., 105, 1858, 3; Hesse, A., 234, 1886, 240; Bauer and Schub, C. A. 23, 1929, 5192. (Pharmacology) Podolsky, see above; Anon., Pract. Dr., 49, Dec., 1931, 31.

Vegetable Dye-stuffs.—Browne, C.A., 23, 1929, 517; Mell, C.A., 24, 1930, 1982.

Chlorophyll.—Willstätter, Jl. Am. Ch. Soc., 37, 1915, 323; Mary, C.A., 9, 1915, 2644; Mazé, C.A., 9, 1915, 3085; Pfeilsticker, C.A., 23, 1929, 413; Robinson, C.A., 23, 1929, 1882; Schwyzer, C.A., 24, 1930, 4897; Ed., Jl. Soc. Ch. Ind., 49, 1930, 884; Fischer, Zt. angew. Ch., 44, 1931, 617; Heilbron, Jl. Soc. Ch. Ind., 50, 1931, 977; Conant and co-workers, Jl. Am. Ch. Soc., 53, 1931, 2382 and 4438.

Carotene.—Kuhn, C.A., 23, 1929, 4682; C.A., 27, 1933, 314 and 750; Ed., Jl. Soc. Ch. Ind., 50, 1931, 103; Rosenheim and Starling, *ibid.*, 50, 1931, 443; Ahmad., *ibid.*, 50, 1931, 4T; Smith, C.A., 25, 1931, 2112; Karrer and co-workers, C.A., 25, 1931, 4531 and 4532 and 26, 1932, 733; Armstrong, Jl. Soc. Ch. Ind., 52, 1933, 53; von Euler and Jansson, C.A., 26, 1932, 162; Brissemoret, C.A., 26, 1932, 171.

Anthocyans.—Willstätter, C.A., 10, 1916, 2216 and 11, 1917, 1404; Ed., Jl. Soc. Ch. Ind., 49, 1930, 696.

Porphyrins.—Fischer, B., 60B, 1927, 2611.

Other Natural Colors.—(General) Willstätter, Ch. and Dr., 87, 1915, 765; Oesterle, Sch. Wsch. Ch. Ph., 50, 1912, 121 and 137; Schwertschlager, C.A., 7, 1913, 3990; Wurdack, Jl. A.Ph.A., 13, 1924, 307 and 399; Moir, C.A., 22, 1928, 2962; Ed., Jl. Soc. Ch. Ind., 48, 1929, 724; Shriner and Anderson, C.A., 23, 1929, 837; Kuroda, C.A., 23, 1929, 1906; Schmid and co-workers, C.A., 26, 1932, 5570; Sando, Jl. Ind. Eng. Ch., News Ed., 9, 1931, 338; Robinson, Jl. Soc. Ch. Ind., 50, 1931, 46 and C.A., 26, 1932, 5307. (Carminic acid) Dimroth, B., 42, 1909, 1613; A., 399, 413, 1; B., 53, 1920, 471. (Orcein) Zulkowski and Peters, B., 23, 1890, R647; Beringer, Jl. A.Ph.A., 1, 1912, 826. (Hematoxylin) Oesterle, see above; Bollina and co-workers, B., 35, 1902, 1678; Perkin and co-workers, Jl. Ch. Soc. Trans., 93, 1908, 489; Pfeiffer and co-workers, C.A., 22, 1928, 425 and 2360; 23, 1929, 150 and 25, 1931, 1533; Anon., Jl. Soc. Ch. Ind., 48, 1929, 1011. (Curcumin) Jackson and Menker, Am. Ch. Jl., 6, 1884, 77; Ghosh, Ch. Soc. Trans., 115, 1919, 292; Lampke and Milobedzka, C.A., 7, 1913, 3333. (Flavone) Kostanecki, B., 31, 1898, 710; 32, 1899, 326; 33, 1900, 330; 37, 1904, 773 and 2634; Willstätter, Jl. Am. Ch. Soc., 37, 1915, 323 and Ch. and Dr., 87, 1915, 765. (Quercetin) Viehoever, Chernoff and Johns, Jl. Agric. Res., 13, 1918, 345; Malkin and Nierenstein, Jl. Am. Ch. Soc., 52, 1930, 2864. (Hesperetidin) Oesterle, Arch. Pharm., 253, 1915, 383. (Chrysoeriol) Power and Tutin, Jl. Ch. Soc., 95, 1909, 81; Oesterle, C.A., 13, 1919, 1361. (Azulene) Scherndal, Jl. Am. Ch. Soc., 37, 1915, 167; Trier, Pharm. Era, 49, 1916, 193; Kremers, Jl. Am. Ch. Soc., 45, 1923, 717. (Bilirubin) Fischer and Rose, C.A., 8, 1914, 1765. (Lapachol) Fieser, Jl. Am. Ch. Soc., 49, 1927, 857. (Xanthophyll) Karrer and co-workers, C.A., 25, 1931, 519.

CHAPTER XLIX

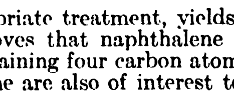
CONDENSED BENZENES AND THEIR DERIVATIVES

WITH the derivatives of the terpenes we close those benzene derivatives which are of interest to pharmacy, and are prepared to take up a new group of the hydrocarbons. These are found in the condensed benzenes—naphthalene and anthracene. Both of these substances are constituents of coal tar, and are obtained by the fractional distillation of this product. The fraction distilling between 180° and 200° C. contains naphthalene, while that coming over from 340° to 360° C. contains anthracene.

Naphthalenum, U.S.P. VIII (*naphthalene* or *naphthalin*) was discovered by Garden in 1819 in coal tar. While naphthalene is always obtained commercially from coal tar, its synthesis has been frequently accomplished. Thus, if methane, ethylene, and acetylene be passed through red-hot tubes, one of the products of this treatment is naphthalene. Other syntheses throwing light on chemical formula are matters of passing interest. Thus if the vapor of phenyl butylene dibromide,

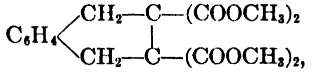
$$C_6H_5CH_2CH_2CHBrCHBr,$$

be passed over red-hot lime, naphthalene results. This synthesis is of importance as showing that naphthalene contains a benzene nucleus. Still more important is the formation of naphthalene from combination of orthoxylene bromide, $C_6H_4\begin{matrix} \diagup CH_2Br \\ \diagdown CH_2Br, \end{matrix}$ with the sodium salt of acetylene tetracarbonic acid methyl ester,



$$\begin{array}{l} Na—C—(COOCH_3)_2 \\ \quad\;\; | \\ Na—C=(COOCH_3)_2. \end{array}$$

When they are brought together, we obtain hydronaphthalene-tetracarbonic methyl ester,

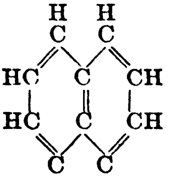


$$C_6H_4\begin{matrix} \diagup CH_2—C—(COOCH_3)_2 \\ \quad\;\; | \\ \diagdown CH_2—C—(COOCH_3)_2, \end{matrix}$$

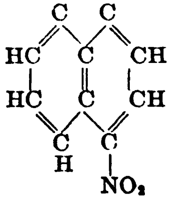
and this substance, with appropriate treatment, yields naphthalene. The importance of this synthesis is that it proves that naphthalene consists of the benzene group, attached to which is a ring containing four carbon atoms.

Two reactions of naphthalene are also of interest to us in helping to establish the formula. The first is that, on oxidation, it breaks up, yielding phthalic acid, $C_6H_4\begin{matrix} \diagup COOH \\ \diagdown COOH \end{matrix}$; and the second is that, when treated with reducing agents, it easily absorbs four atoms of hydrogen and then with difficulty absorbs six more. All these reactions point to the following graphic formula for naphthalene (*a*):

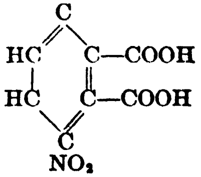
a



b

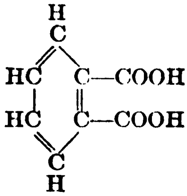


c

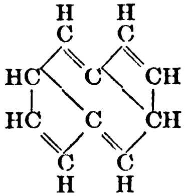


That it contains at least one benzene group is shown by the two syntheses given above. That the added ring containing four carbon atoms is in the ortho position to the benzene group is shown by the second synthesis given above, and also by the oxidation with phthalic acid. That the ring containing four carbon atoms has two double bonds

is shown by the fact that it easily adds four hydrogen atoms; that the extra four carbon atoms are in a ring is shown by the behavior of its mononitro-derivative (*b*). Under certain treatment the pure benzene ring breaks, and we get nitrophthalic acid (*c*). Under other treatment it is the nitro ring that breaks, and we get pure phthalic acid,



From *x*-ray crystal photographs, Shearer deduces the following formula for naphthalene:



Naphthalene has been used considerably under the name of *coal-tar camphor*, and the popular form in which it is sold in the shape of small balls is called *mothballs*. It is used as an insecticide as is camphor, but there is no question as to preference of the aromatic odor of camphor to the rank, persistent odor of naphthalene.

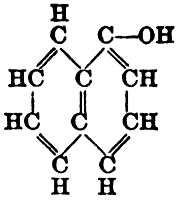
Naphthalene possesses antiseptic properties, and has been recommended as a remedy in chronic bronchitis and intestinal catarrh. Its chief use, however, is externally as an antiseptic dressing, and even for this purpose it is not very popular on account of its disagreeable odor.

Hydrogenated Naphthalenes, such as *tetralin* (tetrahydronaphthalene) and *dekalin* (dekahydronaphthalene), are liquids and are used in Europe as turpentine substitutes in the varnish industry.

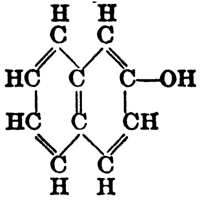
NAPHTHOLS

These are phenols of naphthalene. While there was but one phenol yielded from benzene—phenol, or carbolic acid, U.S.P.—there are two phenols from naphthaleine; for, as shown in the following graphic formula, there is a difference whether the hydroxyl group is placed on the carbon atom next to the pure benzene ring or on the second carbon atom from the same. When placed on the first carbon atom, the derivative is called alpha-naphthol, whereas if placed on the second carbon atom, it is called beta-naphthol. What is true as far as alpha- and beta-naphthol are concerned is true in regard to all the mono-derivatives of the naphthols; two of each derivatives, alpha and beta, being possible.

Alpha-naphthol



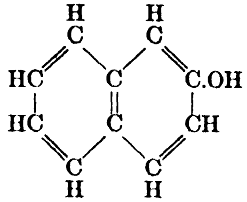
Beta-naphthol



Both naphthols are found in coal tar, and both can be made synthetically by treatment of naphthalene with concentrated sulfuric acid, when the naphthalene-sulfonic acid is produced. If the temperature is carefully kept at 160° C., the product will be the "beta" derivative; alpha-naphthalene-sulfonic acid not being produced when the mixture is heated above 80° C. If this "beta" derivative is fused with sodium hydroxide, betanaphthol results.

BETANAPHTHOL—Betanaphthol
(Betanaph.)

$C_{10}H_8O$



Molecular weight, 144.06

Betahydroxynaphthalene.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, or pale buff-colored shining crystalline leaflets, or white or yellowish-white crystalline powder; faint phenol-like odor; pungent taste; soluble in about 1000 parts of water and in about 0.6 part of alcohol; also soluble in chloroform, ether, glycerin, olive oil and in alkali hydroxide solutions; melts between 120° and 122° C., sublimes readily on heating. For details, see U.S.P., p. 87.

For *tests for identity*, for *impurities* (naphthalene, other organic matter, alpha-naphthol), see U.S.P., p. 87.

Remarks.—Betanaphthol is used as an antiseptic both internally and externally, a solution of 1:1000 being a good germicide. It is given internally in intestinal troubles, especially in typhoid fever, and has recently been recommended in hookworm disease.

Incompatibilities.—See prescription No. 75 in Chapter LIX.

Dose.—250 mg. (4 grains).

Naphthol itself possesses rather irritating properties, and has a decidedly peppery taste. For that reason its application is somewhat limited, and many efforts have been made to prepare derivatives that are equally valuable as antiseptics and possessing less irritating properties. Among these derivatives are found the following:

Bismuthi Betanaphtholas (U.S.P. IX) is prepared by precipitating a solution of sodium betanaphtholate with an acetic acid solution of bismuth nitrate. It is a popular intestinal antiseptic; one commercial form of which is marketed under the name, *orphol*. *Dose.*—500 mg. (8 grains).

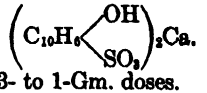
Betol is naphthol salol or naphthol salicylate, $C_{10}H_7OOCC_6H_4OH$, and is made by treatment of the betanaphthol sodium compound with salicylic acid, in the presence of phosphorus oxychloride. The action of betol is similar to salol, except that when it enters the intestines it decomposes into naphthol instead of phenol.

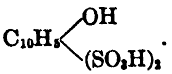
Betol is given in doses of 1 Gm.

Alphanaphthol.—This naphthol derivative is said to act as a germicide in the proportion of 1:4000, and is also said to be one third as poisonous as is betanaphthol. *Dose.*—1 Gm.

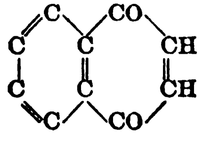
Benzonaphthol.—This is betanaphthol benzoate, and is, therefore, the benzoic acid ester of naphthol, and is prepared by combining naphthol with benzoyl chloride. It is a valuable intestinal antiseptic, and given in 1-Gm. doses.

Naphtholaristol.—Di-iodo-betanaphthol. This is an iodine derivative of naphthol, and is used as an antiseptic, under the name *iodonaphthol*.

Asaprol.—This is a calcium betanaphthol monosulfonate,  $\left(C_{10}H_6\begin{matrix}\diagup OH\\ \diagdown SO_3\end{matrix}\right)_2Ca$. It is sometimes called *abrastol*, and is used as an antipyretic in 0.3- to 1-Gm. doses.

Alumnol is aluminum betanaphthol disulfonate; that is, the aluminum salt of the acid,  $C_{10}H_5\left\langle\begin{matrix}OH\\(SO_3H)_2\end{matrix}\right.$. It is used as an astringent and antiseptic, almost entirely externally.

Naphtho Quinones.—These exist in the alpha and beta forms. The alpha variety has the formula



and yields several important dye-stuffs.

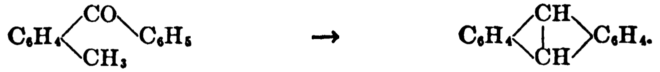
Naphthylamine, $C_{10}H_7NH_2$, is the amino derivative of naphthol, bearing the same relation to it as aniline does to phenol. Its acetate and hydrochloride are used in water testing (p. 414).

Bayer 205 is the urea compound of meta-amino-para-methylbenzoyl-naphthylamine trisulfonate of sodium. It is claimed to be a specific in sleeping sickness.

ANTHRACENE

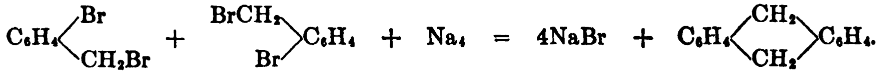
Formula, $C_{14}H_{10}$. This substance, which was discovered by Dumas and Lamant in 1835, is of importance in pharmacy only because of its medicinal derivatives. The substance itself is found in coal tar, and is obtained from same by fractional distillation. It can also be made by passing simple organic substances, such as methane, ethylene, or alcohol, through red-hot tubes.

Three syntheses of anthracene are worthy of mention as establishing the structural formula of the body. The first synthesis is its production, by treatment of orthotolylphenyl-ketone, with zinc dust. This reaction is best shown by the following graphic equation:



$$C_6H_4\left\langle\begin{matrix}CO\\CH_3\end{matrix}\right\rangle C_6H_5 \quad\longrightarrow\quad C_6H_4\left\langle\begin{matrix}CH\\|\\CH\end{matrix}\right\rangle C_6H_4.$$

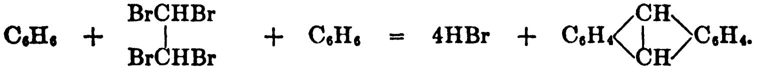
It can also be made from orthobrombenzyl bromide, treating same in ethereal solution with sodium, thus removing the bromine, with the formation of hydroanthracene:



$$C_6H_4\left\langle\begin{matrix}Br\\CH_2Br\end{matrix}\right. + \left.\begin{matrix}BrCH_2\\Br\end{matrix}\right\rangle C_6H_4 + Na_4 = 4NaBr + C_6H_4\left\langle\begin{matrix}CH_2\\CH_2\end{matrix}\right\rangle C_6H_4.$$

And this, when treated with an oxidizing agent, yields anthracene.

A third synthesis of anthracene is by treating benzene with tetrabromethane in the presence of aluminum chloride, as is shown in the equation given below:



$$C_6H_6 + \begin{matrix}BrCHBr\\|\\BrCHBr\end{matrix} + C_6H_6 = 4HBr + C_6H_4\left\langle\begin{matrix}CH\\|\\CH\end{matrix}\right\rangle C_6H_4.$$

It may be recalled that naphthalene, when treated with nascent hydrogen, easily adds four atoms of hydrogen, and with difficulty six more were persuaded to go on. Anthracene, likewise, easily adds four atoms of hydrogen, and under additional treatment it can be made to take up ten extra atoms of hydrogen, this seeming to point to the existence of seven double bonds, two of which are more easily replaceable than the other five.

The structure of anthracene is deduced from the following considerations:

First, it must possess two benzene rings, this being proved by the synthesis of orthotolylphenyl ketone and by the hydroanthracene synthesis.

Secondly, the middle ring proceeds from the ortho position of both benzenes; this being proved by the synthesis with orthobrombenzyl bromide.

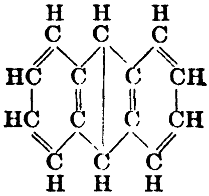
Thirdly, the middle ring has an ethylene bond extending between its two individual carbon atoms; this is shown by the hydro-anthracene synthesis.

Fourthly, this ethylene bond is weaker than the others, as shown by the ease with which the two hydrogens are added.

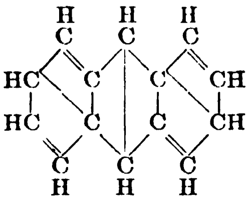
Fifth, that each of the two benzene rings have three ethylene bonds; this being proved by the fact that the body absorbs ten other atoms of hydrogen, but that with more difficulty than did the first two.

From these facts the accepted formula of anthracene has been "I" given below; but from a study of *x*-ray crystal photographs, Shearer has deduced formula "II" given below:

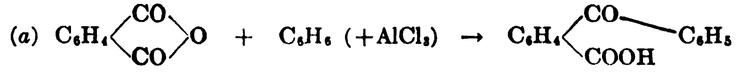
I



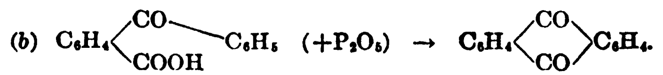
II



Anthraquinone.—Formula, $C_{14}H_8O_2$. This is an anthracene derivative in which two hydrogen atoms have been replaced by two oxygen atoms. It is made by the treatment of phthalic acid anhydride with benzene in the presence of aluminum chloride, this yielding orthobenzoyl benzoic acid, which substance is converted into anthraquinone when treated with phosphorus pentoxide:

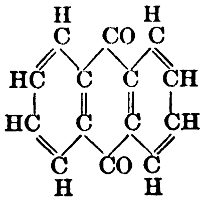


$$(a)\ C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle O + C_6H_6\ (+AlCl_3) \rightarrow C_6H_4\left\langle\begin{matrix}CO\text{——}C_6H_5\\COOH\end{matrix}\right.$$

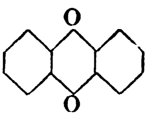


$$(b)\ C_6H_4\left\langle\begin{matrix}CO\text{——}C_6H_5\\COOH\end{matrix}\right.\ (+P_2O_5) \rightarrow C_6H_4\left\langle\begin{matrix}CO\\CO\end{matrix}\right\rangle C_6H_4.$$

This reaction led to the conclusion that the graphic formula of anthraquinone is

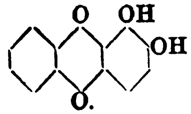


or, schematically,



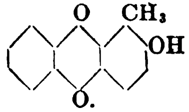
Anthraquinone can also be made by the oxidation of anthracene with chromic acid.

Anthraquinone is of little importance in pharmacy, but the oxy-derivatives of it are worth more than passing notice. Among these we find *alizarine*, which is *dioxyanthraquinone:*



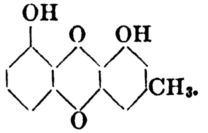
This substance, which is a coloring constituent of madder, was isolated from that dye-stuff by Graebe and Lieberman in the year 1867. In 1879 these investigators accomplished its synthesis by treating phthalic acid anhydride with pyrocatechin. *Madder* is the ground root of *Anchusa tinctoria*, and formerly one of the staple dyeing materials was an infusion of this substance, which yielded, in the presence of aluminum salts, characteristic scarlet dyes. The madder industry represented an important item in the agriculture of southern France until the discovery of synthetic alizarine, since which time the industry has been practically ruined.

Oxy-methylanthraquinone,



This substance was discovered by Tschirch in his valuable researches of the active principles of the well-known purgative resins, and considered by him as the fundamental purgative principle.

Dioxymethylanthraquinone (*chrysophanic acid* or *chrysophanol*),

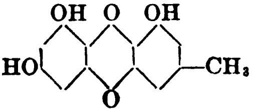


This substance represents an active purgative principle of chrysarobin, senna, rhubarb, cascara sagrada. Note that this is not the chrysophanic acid of commerce, that name being erroneously applied to the natural product which the Pharmacopœia calls chrysarobin (p. 896).

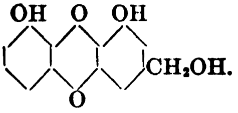
Trioxymethylanthraquinone, or *emodin.* This is one of the important purgative principles found in rhubarb, frangula, and aloes.

According to Oesterle, the emodins from these three sources are not identical, differing in the exact location of the methyl and hydroxyl groups. Thus rhubarb-emodin he considers as having formula I (below) while aloe-emodin he thinks has formula II.

I

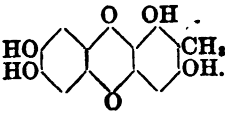


II



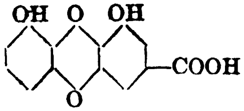
Emodin has been prepared synthetically.

Tetraoxymethylanthraquinone,



Tetraoxymethylanthraquinone is called *aloexanthin*, being one of the less important constituents of aloes. Aloin, according to Tschirch, is pentaoxymethylanthraquinone, but commercial aloin is really a glucosidal mixture. (See p. 895.)

Dioxycarboxyanthraquinone, or *rhein*,



is an important constituent of rhubarb.

DRUGS CONTAINING THE ANTHRAQUINONE PURGATIVES

RHEUM—Rhubarb

Rhubarb consists of the dried rhizome and roots of *Rheum officinale* Baillon or of *Rheum palmatum* Linné (Fam. *Polygonaceæ*) or of other species (excepting Rheum rhaponticum) or of hybrids of *Rheum*, grown in China and Tibet, deprived of periderm tissues.

Rhubarb yields not less than 30 per cent of diluted alcohol-soluble extractive.

Constituents.—Chrysophanic acid; emodin and its methyl ether; rhein, gallic acid and tannin, resin; volatile oil (trace); etc. The resin is a combination of a phytosterol, *verosterol*, with palmitic, oleic, linoleic and linolenic acids.

Remarks.—Rhubarb, one of our most valuable medicines, is the sliced and dried root of *Rheum officinale.* Study its constituents very carefully, noting that, besides the cathartic anthraquinone derivatives, it contains an astringent—rheotannic acid—and, therefore, while the drug, administered alone, has a purgative action, when combined with aromatics it acts as an astringent. This explains why aromatic syrup of rhubarb checks diarrhea, while syrup of rhubarb is a laxative.

The present Pharmacopœia provides tests for the presence of emodin and of chrysophanic acid in rhubarb. The drug is heated with 1 per cent potassium hydroxide solution; the filtrate is acidulated with hydrochloric acid and is then shaken out with ether; the yellow ethereal extract when shaken with ammonia water gives a cherry red ammoniacal layer (emodin) and a yellow ethereal layer (chrysophanic acid).

Torrefied rhubarb (p. 101) is the roasted drug. The purgative anthraquinone bodies are dissipated and the pure astringent results.

Medical Properties.—Cathartic and astringent (see above). Official preparations: *Fluidextract* (N.F. VI) (p. 271), *compound tincture* (N.F. VI) (p. 254), *aromatic tincture* (p. 251), *extract* (p. 302) and *compound powder* (N.F. VI) (p. 316). The *syrup* (N.F. VI) (p. 223) is made from the fluidextract, while the *aromatic syrup* (p. 220) is made from the aromatic tincture.

Dose.—Of drug, 1 Gm. (15 grains).

Frangula (N.F. VI), or *Buckthorn Bark*, is obtained from *Rhamnus Frangula.* It contains *frangulin*; emodin (free and combined); chrysophanic acid (free and combined); rhamnol, a phytosterol; rhamnose (a sugar); etc. Frangulin is a glucoside, hydrolyzing to emodin and rhamnose. It is used as a cathartic in 1-Gm. doses. The Formulary recognizes the *fluidextract* (p. 271).

CASCARA SAGRADA—Cascara Sagrada

(Casc. Sagr.—Rhamnus Purshiana)

Cascara Sagrada is the dried bark of *Rhamnus Purshiana* De Candolle (Fam. *Rhamnaceæ*).

Cascara Sagrada contains not more than 4 per cent of foreign organic matter and should be collected at least one year before being used for making medicinal preparations.

Constituents.—Chrysophanic acid, emodin, bitter resins, etc.

Remarks.—Cascara sagrada is one of our most popular purgatives. Its chief drawback is its bitter taste, but it has been found that the bitterness resides largely in a resinous principle, and can be removed by treatment with alkali, without seriously lessening the purgative action of the drug. This fact is applied in the manufacture of the official aromatic fluidextract, where the bark is freed from bitterness by treatment with magnesium oxide.

Both frangula and cascara sagrada in fresh condition contain an enzyme which causes griping, and which is dissociated on allowing the bark to age; hence the Pharmacopœia requirement required that both barks be at least one year old when used. It is claimed, however, that heating the bark for a few hours at 100° C. destroys the ferment, and that barks can, therefore, be aged in this way.

Medical Properties.—Purgative of great service. There is, however, danger of contracting the "cascara habit." The *extract* (p. 300), *fluidextract* (p. 268), and the *aromatic fluidextract* (p. 268) are official.

Dose.—1 Gm. (15 grains).

SENNA—Senna

(Senn.—Senna Leaves)

Senna consists of the dried leaflets of *Cassia Senna* Linné, known in commerce as Alexandria Senna, or of *Cassia angustifolia* Vahl, known in commerce as Tinnevelly Senna (Fam. *Leguminosæ*).

Senna contains not more than 8 per cent of its stems, and not more than 2 per cent of its pods or other foreign organic matter, and yields not more than 3 per cent of acid-insoluble ash.

Constituents.—*Rhein, aloe-emodin* and their glucosides; *kæmferol* (a trihydroxy-flavenol) and its glucoside; volatile oil (trace); resins; salicylic acid; etc.

The resins are combinations of a phytosterol and a phytosterolin, with fatty acids (palmitic, stearic, etc.). Cathartic acid of older investigators is now known to be a mixture. The ash of Tinnevelly senna contains considerable magnesium. Alexandrian senna has the same constituents as Tinnevelly except it contains some iso-rhamnetic acid and no magnesium.

Remarks.—Senna represents the leaflets of two plants, *Cassia Senna* being the source of the drug shipped from Egypt, and *Cassia angustifolia* yielding that exported from India. *Tinnevelly Senna* is a fine variety coming from India. Strong alcohol removes the griping, resinous principle without extracting the true purgative constituent, and this idea was employed in the recipe for the fluidextract given in the last Pharmacopœia.

Medical Properties.—Cathartic. Official preparations: The *fluidextract* (p. 266), *syrup of senna* (p. 221) which is made from the fluidextract. Senna is a constituent of *compound powder of senna* (p. 316).

Dose.—Of drug, 2 Gm. (30 grains).

ALOE—Aloe

(Aloes)

Aloe is the dried juice of the leaves of *Aloe Perryi* Baker, known in commerce as Socotrine Aloe, or of *Aloe vera* Linné, known in commerce as Curaçao Aloe (Fam. *Liliaceæ*).

Aloe yields not more than 4 per cent of ash, not more than 10 per cent of moisture, and not less than 50 per cent of water-soluble extractive.

Constituents.—Aloin; emodin; resin; volatile oil (trace), etc.

Remarks.—It will be noted that the official definition given above mentions two sources of aloe (or aloes, as we have hitherto called this drug. The plant *Aloe vera* furnishes Curaçao aloe, *Aloe Perryi* yields Socotrine aloe. In U.S.P. X, Cape aloe, from *Aloe ferox* was also official. The aloins from these three varieties are not identical.

In passing it might be stated that these plants have large succulent leaves, like those of the century plant, and that the drug is obtained by cutting these leaves from their base, allowing the juice to drain (in poorer varieties the leaves are expressed), and permitting it to dry in the sun.

Up to now, no satisfactory chemical assay for aloe has been devised. Viehoever, however, finds in the crustacean, *Daphnia pulex*, an admirable biologic test-animal for determining the therapeutic effect of anthraquinone purgatives.

Medical Properties.—Laxative, purgative, emmenagogue. Official preparation: *pills* (p. 340). Aloe is also a constituent of *compound extract of colocynth* (N.F. VI) (p. 303), and *compound tincture of benzoin* (p. 245).

Dose.—250 mg. (4 grains).

Aloe Purificata (U.S.P. VIII) is aloe purified by mixing with enough alcohol to make a liquid that can be strained through a No. 60 sieve, and the strained liquid is then freed from alcohol by evaporation on a water bath. In other words, the process is purely mechanical, the object being to free crude aloes from dirt, straw, and other insoluble impurities. In the past, commercial aloes was so impure that purification was imperative, but thanks to the pure food and drug law and the more rigid inspection of drugs as they pass through the ports of entry, the quality of aloe has greatly improved.

ALOINUM—Aloin

(Aloin.)

Aloin is a pentoside or mixture of pentosides obtained from aloe. It varies in chemical composition and in physical and chemical properties according to the variety of aloe from which it is obtained.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Micro-crystalline powder or minute acicular crystals; color, lemon-yellow to dark yellow; not more than faint odor of aloe; intensely bitter taste; darkens on exposure to light and air; soluble in water, alcohol and acetone; slightly soluble in ether. For details, see U.S.P., p. 48.

For *tests for identity* and for *impurity* (emodin), see U.S.P., p. 48.

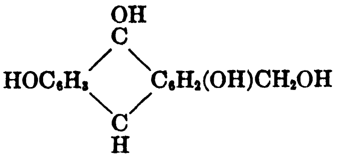
Extraction.—Aloe is treated with acidulated hot water and the infusion allowed to stand a day; the clear liquid is decanted from the sediment, concentrated at low heat, and set in a cool place, when the aloin will separate in minute crystals. This crude aloin is then purified by recrystallization from hot water. It is also made by treating an acid infusion of aloes with alkali and solution of calcium chloride. A combination of aloin with calcium is effected, and this separates out, the calcium being eventually removed by solution in diluted hydrochloric acid. The mixture is then treated with hot water, in which the resulting calcium chloride is very soluble, while the less soluble aloin crystallizes from the solution on cooling.

Composition.—There has been much controversy as to the structure of the aloins. Present information may be summarized as follows:

1. The aloins are pentosides; that is glucosidal combinations of the pentoses with anthraquinone compounds.
2. Rosenthaler states that barbaloin hydrolyzes according to the following equation:

$$\begin{array}{ccccccc} & & & & \text{Aloe-emodin} & & \\ \text{Aloin} & & & & \text{anthranol} & & \text{Arabinose} \\ C_{20}H_{20}O_8 & + & H_2O & = & C_{15}H_{12}O_4 & + & C_5H_{10}O_5 \end{array}$$

3. The anthranol apparently has the formula:



Remarks.—While in U.S.P. VIII, the aloin from Curaçao aloe was given the preference, in the present edition, any of the several aloins can be employed. Hence there has been omitted Histed's test, that well-known reaction based upon the behavior of the several forms of aloin when treated with concentrated nitric acid. With this reagent Curaçao aloin and Barbadoes aloin turn cherry red; nataloin (that from Natal aloe) turns vivid crimson; socaloin (that from Socotrine aloe) is not colored; while capaloin (that from Cape aloe) turns a permanent green.

Medical Properties.—Purgative.

Dose.—15 mg. (¼ grain).

CHRYSAROBINUM—Chrysarobin

(Chrysarob.)

Chrysarobin is a mixture of neutral principles obtained from Goa powder, a substance deposited in the wood of *Vouacapoua Araroba* (Aguiar) Druce (Fam. *Leguminosæ*).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Brownish to orange-yellow, micro-crystalline powder; irritating to the mucous membrane; soluble in about 4800 parts of water and in about 310 parts of alcohol; also soluble in chloroform, ether, benzene and carbon disulfide. For details, see U.S.P., p. 121.

For *tests for identity* and for *impurity* (chrysophanic acid), see U.S.P., p. 121.

Constituents.—Emodin, chrysophanic acid, emodin monomethyl ether, anthranol of emodin monomethyl ether, anthranol of chrysophanic acid, ararobinol, $C_{23}H_{16}O_5$, sugar, etc.

Extraction.—Chrysarobin is obtained from Goa powder by extraction with hot chloroform, evaporation of the chloroformic solution to dryness, and powdering the residue.

Remarks.—*Chrysarobin,* long and improperly called *chrysophanic acid,* is a derivative of Goa powder, a waste product of the tree *Vouacapoua Araroba.* While excellent for skin diseases, chrysarobin is objectionable by reason of the stain it produces.

Medical Properties.—Drastic purgative. Generally used externally in skin troubles in the form of the official *ointment* (p. 366).

BIBLIOGRAPHY

Naphthalene.—(Preparation and properties) Kidd, Ann. de chim. et phys., 19, 1821, 273; Laurent, A., 3, 1832, 9; von Skopnik, Jl. Soc. Ch. Ind., 46, 1927, 358B. (Structure) Graebe, A., 149, 1869, 22; Weinberg, C.A., 16, 1921, 1090; Shearer, Jl. Soc. Ch. Ind., 41, 1922, 562R. (Syntheses) Berthelot, A., 141, 1867, 182; Aronheim, B., 6, 1873, 67; Radziszewski, B., 9, 1876, 261; Baeyer and Perkin, B., 17, 1884, 488. (Reactions) Laurent, A., 19, 1836, 38; Marignac, A., 38, 1841, 13. Heusler, B., 28, 1895, R., 490; Wreden and Znatowitcz, B., 9, 1876, 278 and 591. (Uses) Markoe, A.Ph.A., 17, 1869, 365.

Hydrogenated Naphthalenes.—Frydlender, C.A., 14, 1920, 3231; Furness, *ibid.*, 16, 1922, 2141; Sadtler, A.J.P., 95, 1923, 282; Inoue, C.A., 18, 1924, 2697; Zelinski, Jl. Soc. Ch. Ind., 44, 1925, 66B.

Naphthols.—(Structure) Liebermann, A., 183, 1876, 254 and B., 15, 1882, 1427. (Preparation) Merz and Werth, B., 4, 1870, 195. (Therapeutics) Smillie, C.A., 14, 1920, 3473; Cains and Mhaskar, *ibid.*, 16, 1922, 1113.

Betanaphthol.—Bouchard, Ph. Jl., [3], 18, 1887, 457.

Alphanaphthol.—Anon., A.J.P., 59, 1887, 566; Maximovitch, Comp. rend., 106, 1888, 366.

Betol.—Robert, Arch. d. Pharm., 226, 1888, 703.

Benzonaphthol.—Berlioz, A.Ph.A., 40, 1892, 951; Griggi, Merck's Rep., 3, 1894, 288.

Hydronaphthol.—Anon., Jl. A.M.A., 55, 1910, 878.

Asaprol.—Stackler, A.J.P., 64, 1892, 517.

Alumnol.—Anon., A.Ph.A., 41, 1893, 503.

Naphtho Quinones.—Groves, A., 167, 1873, 357; Liebermann and Jacobson, A., 211, 1882, 36.

Bayer 205.—Fourneau and co-workers, C.A., 18, 1924, 2764; Heymann, C.A., 18, 1924, 3219.

Anthracene.—(Source) Dumas and Lamant, A., 5, 1833, 10; Laurent, A., 34, 1840, 237. (Structure) van Dorp, A., 169, 1873, 219; Shearer, Jl. Soc. Ch. Ind., 41, 1922, 562R. (Syntheses) Behr and van Dorp, B., 7, 1873, 16; Jackson and White, B., 12, 1879, 1965; Anschutz and Eltzbacher, B., 16, 1883, 623.

Anthraquinone.—(Structure) Graebe and Liebermann, A., Supp. 7, 1870, 285; van Dorp, see above; Tschirch, see below. (Syntheses) Heller, Zt. angew. Ch., 19, 1906, 669.

Alizarin.—(Structure) Graebe and Liebermann, see above. (Syntheses) Graebe and Liebermann, B., 2, 1869, 332; Baeyer and Caro, B., 7, 1874, 972.

Madder.—Marre, Rev. chim. ind., 18, 1908, 204.

Oxymethyl Anthraquinones.—Tschirch, Ber. d. Pharm. Ges., 8, 1898, 174; Oesterle, Arch. d. Pharm., 249, 1911, 445 and 250, 1912, 301; Jacobson and Adams, Jl. Am. Ch. Soc., 46, 1924, 1312.

Rhubarb.—(Source) Ward, Ph. Jl., 126, 1931, 105. (Constituents) Tutin and Clewer, Jl. Ch. Soc., 99, 1911, 946.

Frangula.—(Constituents) Binswanger, Repert. Pharm., [3], 4, 1850, 145; Buchner, A., 87, 1853, 218; Faust, Arch. d. Pharm., 187, 1869, 18; Liebermann and Waldheim, B., 9, 1876, 1775; Oesterle and Tisza, Arch. d. Pharm., 246, 1908, 112; Beal and Gunton, Jl. A.Ph.A., 11, 1922, 669; Casparis and Raeder, Jl. Soc. Ch. Ind., 44, 1925, 898B; Roulief and Dubreuil, C.A., 23, 1929, 4014.

Cascara Sagrada.—(History) Lloyd, A.Ph.A., 59, 1911, 258; Zwerg, Pharm. Era, 34, 1905, 150. (Collection) Johnson and Hindman, A.J.P., 86, 1914, 387. (Pharmacognosy) Gathercoal, Jl. A.Ph.A., 4, 1915, 65; Starker and Wilcox, A.J.P., 103, 1931, 73 and 147. (Constituents) Limousin, A.J.P., 57, 1885, 205; Schwabe, A.J.P., 60, 1888, 515; Wenzell, A.J.P., 58, 1886, 252; Prescott, A.J.P., 51, 1879, 166; Tschirch, Arch. d. Pharm., 250, 1912, 92; Peacock, Jl. A.Ph.A., 15, 1926, 639. (Pharmacology) Harris and Davy, Jl. A.Ph.A., 19, 1930, 28; Hoch, A.J.P., 105, 1933, 64. (Griping ferment) Aweng, A.Ph.A., 46, 1898, 867. ("Tasteless cascara") Grozer, A.Ph.A., 36, 1888, 402; Gilpin, A.Ph.A., 44, 1896, 421.

Senna.—(History) Joensson, Pharm. Era, 56, 1923, 607. (Sources) Batka, A.J.P., 21, 1849, 358; Dilly, Am. Dr., 23, 1893, 13. (Constituents) Tutin, Jl. Ch. Soc., 103, 1913, 2006. (Non-griping) Diehl, Ph. Jl., [3], 6, 1876, 744.

Aloe.—(History) Schoff, Jl. Am. Oriental Soc., 42, 1922, 171; Anon., Ph. Era, 67, 1930, 278. (Source) Baker, A.Ph.A., 39, 1891, 371; Kebler, Am. Dr., 46, 1902, 162; Miller, Jl. A.Ph.A., 1, 1912, 877; Tschirch, Ch. and Dr., 62, 1903, 664; Marloth, C.A., 22, 1928, 2033; Bryant, Ph. Jl., 130, 1933, 174. (Collection) Pereira, A.J.P., 24, 1852, 231; Groves, A.J.P., 29, 1857, 142. (Constituents) Pereira, Groves, see above; Tilden, Ph. Jl., [3], 1, 1870, 375 and [3], 2, 1872, 845; Leger, A.Ph.A., 58, 1910, 379; Oesterle and Riat, A.Ph.A., 58, 1910, 379 and 381; Tutin and Naunton, Ph. Jl., 91, 1913, 836; Engelhardt and Crosbie, Jl. A.Ph.A., 12, 1923, 695. (Tests) Ware, Jl. Soc. Ch. Ind., 44, 1925, 782B and Ph. Jl., 124, 1930, 596; Schorn, *ibid.*, 124, 1930, 212 and 219; Viehoever, A.J.P., 107, 1935, 47.

Purified Aloe.—Procter, A.J.P., 36, 1864, 300.

Aloin.—(Structure) Rosenthaler, C.A., 24, 1930, 4900; C.A., 26, 1932, 3332; C.A., 26, 1932, 3621; Arch. Pharm., 270, 1932, 214; C.A., 27, 1933, 162; Leger, C.A., 25, 1931, 2141; Simonsen and co-workers, C.A., 24, 1930, 2752 and 27, 1933, 95; Gerecs, C.A., 25, 1931, 2732; Mitter and Banerjee, C.A., 27, 1933, 500. (Fxtraction) Tilden, A.J.P., 43, 1871, 34; Mitchell, A.J.P., 48, 1876, 24. (Histed's test) Flückiger, Arch. d. Pharm., 199, 1872, 15.

Chrysarobin.—(Sources) Lima, Ph. Jl., [3], 5, 1875, 723; Holmes, Ph. Jl., [3], 5, 1875, 801 and 816. (Constituents) Attfield, Ph. Jl., [3], 5, 1875, 721; Tutin and Clewer, Jl. Ch. Soc., 101, 1912, 290; Eder, Arch. d. Pharm., 253, 1915, 1 and *ibid.*, 263, 1925, 321; Eder and Hauser, C.A., 20, 1926, 411; Gardner, C.A., 26, 1932, 5558. (Therapeutics) Schamberg, Raiziss and Kolmer, C.A., 9, 1915, 2672.

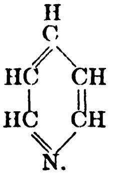
CHAPTER L

THE PYRIDINE AND QUINOLINE DERIVATIVES

It may be recalled (p. 764), that we have already considered a nitrogen compound, pyrrol, having the formula C_4H_4N. Pyridine is a ring compound similar to pyrrol, but having the formula C_5H_5N. It occurs in coal tar, and has the disagreeable odor of bone oil.

It can be made by treating piperidine with concentrated sulfuric acid at a temperature of 300° C.; piperidine, $C_5H_{11}N$, being made by heating pentamethylene-diamine hydrochloride. It can also be made from quinoline.

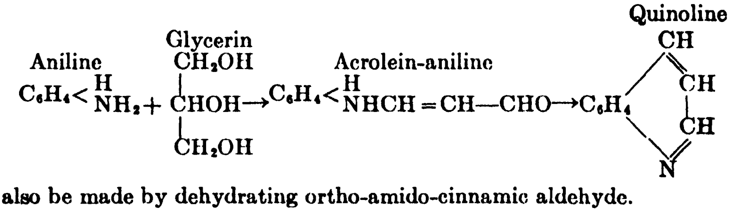
Pyridine resembles benzene in being oxidized with difficulty, and having the power to absorb 6 atoms of hydrogen or of any halogen. From this behavior and other reactions it is assumed that the formula of pyridine resembles that of benzene, except that in place of one of the carbon atoms in the benzene ring an atom of nitrogen is substituted, giving the graphic formula—



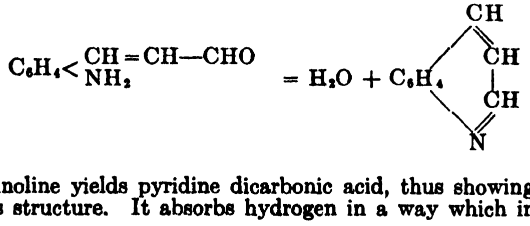
Pyridine is a colorless liquid, which, on account of its nauseating taste, is used for denaturing alcohol—*i. e.*, for adding to alcohol which is to be used in the arts—and is, therefore, permitted to be sold without the revenue tax. The addition of the disagreeable constituent, pyridine, renders the use of such alcohol impossible as a beverage, and therefore accomplishes the purpose desired by the government. Pyridine is also used in asthma by inhalation, and is sometimes administered internally in doses of 2 to 10 minims.

Quinoline, C_9H_7N, is closely allied to pyridine, occurring, like it, in coal tar and also in bone oil.

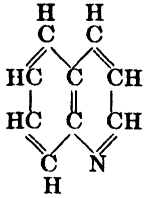
Quinoline is made by Skraup's reaction, which consists of treating aniline with glycerin in the presence of sulfuric acid and nitrobenzene.


Quinoline
Glycerin
Aniline
Acrolein-aniline
$C_6H_4<{H \atop NH_2} +$
CH₂OH
CHOH
CH₂OH
$\rightarrow C_6H_4<{H \atop NHCH=CH—CHO} \rightarrow C_6H_4$
CH
CH
CH
N

It can also be made by dehydrating ortho-amido-cinnamic aldehyde.

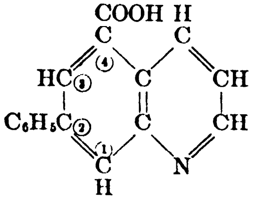


On oxidation, quinoline yields pyridine dicarbonic acid, thus showing that it has a pyridine ring in its structure. It absorbs hydrogen in a way which indicates that not only does it possess a pyridine ring, but also a benzene ring, and to the substance is, therefore, assigned the following graphic formula:



Besides the methods of synthesis of quinoline given above, the chemical has been produced by the fusion of quinine with potassium hydroxide, and it was by this means that the compound was discovered and received its name.

Cinchophenum (U.S.P. X; N.F. VI), or *Phenylcinchoninic Acid,* or *atophan,* has the formula $C_9H_5N.C_6H_5.COOH$ 2 : 4. It is a derivative of quinoline and the figures given in the formula represent the carbon atoms of the quinoline nucleus to which the phenyl and the carboxyl groups are attached. The graphic formula given below makes this more plain.



It is made by condensation of pyroracemic acid (a product of the destructive distillation of tartaric acid) with benzylidine aniline (produced by treating aniline with benzaldehyde).

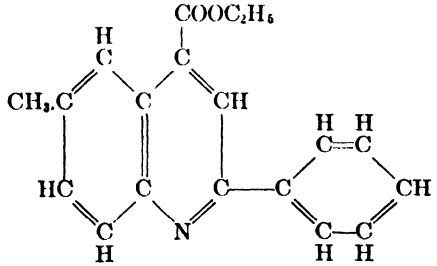
Atophan occurs in colorless needles, melting at 213° to 216° C. It is insoluble in cold water and has a slightly bitter taste. It is used in gout, since it is supposed to increase the uric-acid excretion. Barron has pointed out that it is not devoid of toxicity.

Dose.—500 mg. (8 grains).

NEOCINCHOPHENUM—Neocinchophen

(Neocinchophen.)

$C_{19}H_{17}O_2N$



Molecular weight, 291.14

The ethyl ester of 6-methyl-2-phenylquinoline-4-carboxylic acid.

Summarized Description.

Pale yellow crystalline powder; odorless and tasteless; nearly insoluble in water; soluble in hot alcohol; very soluble in ether and chloroform; melts at not less than 74° C. For details, see U.S.P., p. 242.

For *tests for identity* and for *impurity* (cinchophen), see U.S.P., p. 242.

Remarks.—This new official represents a methylated cinchophen. It is also known as *novatophan.* It has the advantage over cinchophen of being tasteless. It is used like cinchophen.

Dose.—**500 mg. (8 grains).**

PULVIS CHINIOFONI—Chiniofon Powder

(Pulv. Chiniofon.—Chiniofon)

A mixture of 7-iodo-8-hydroxyquinoline-5-sulfonic acid, sodium bicarbonate and sodium iodohydroxyquinolinesulfonate, containing not less than 26.5 per cent and not more than 28.9 per cent of iodine (I).

Storage.—Preserve in bottles having well-fitting, paraffined stoppers.

Summarized Description.

Canary-yellow powder; slight odor; bitter taste turning to sweetish after-taste; dissolves in water with effervescence. For details, see U.S.P., p. 309.

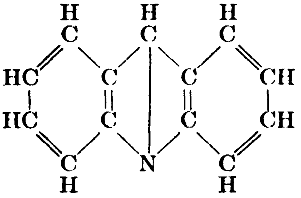
For *tests for identity*, for *impurities* (free iodine and iodide) and for *assay*, see U.S.P., p. 309.

Remarks.—This new official is a mixture of iodohydroxyquinolinesulfonic acid, its sodium salt and sodium bicarbonate. It contains about 27 per cent of iodine. It is recommended in the treatment of amebic dysentery.

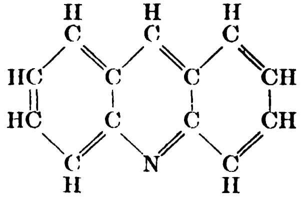
Dose.—1 Gm. (15 grains).

Plasmochin is dimethylamino-iso-pentyl-amino-methoxyquinoline. It has been found of marked value in the treatment of malaria.

Acridine, $C_{13}H_9N$, completes the trio of nitrogenous derivatives corresponding to benzene, naphthalene and anthracene respectively. The structure of acridine is either



or



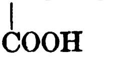
and a comparison of this with the formula of anthracene (p. 890) will show their close relationship.

Acridine is obtained from the anthracene fraction of coal tar and occurs in grayish crystals, which provoke sneezing. It is the basis of a line of dyes of which the following are now enjoying considerable vogue both as wound antiseptics and as specifics for certain micrococci, when injected into the blood stream:

Acriflavine, or *trypaflavine*, diaminomethylacridine chloride (p. 781).
Proflavine, diaminoacridine sulfate.
Rivenol, ethoxyaminoacridine.

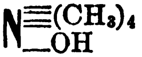
ALKALOIDS

Alkaloids are an important class of plant bases having complex composition; in fact, some chemists considering the phrase "alkaloid" as covering only those basic organic substances whose chemistry is not clearly defined. This statement, while extreme, is partially justified by the fact that, as alkaloidal bodies are studied, they are frequently assigned to other divisions of chemistry. Thus *betaine* from beets is now grouped among the derivatives of glycocoll, or amido-acetic acid,



$$\begin{array}{l} CH_2NH_2 \\ | \\ COOH \end{array}$$

(p. 671); choline from bile is classed as a derivative of tetramethyl ammonium hydroxide,



$$N\begin{array}{l}\equiv(CH_3)_4 \\ -OH\end{array}$$

(p. 638); while caffeine is now considered as a uric-acid derivative (p. 759) the Pharmacopœia dropping the word "alkaloid" in discussing it. There still remains, however, a distinct class of bodies which we can call alkaloids; the present definition for alkaloids being ***nitrogenous plant bases, which are derivatives of pyridine, quinoline, or similar ringed bodies.***

Hence it is necessary to drop the old classification of alkaloids and turn to the new, but before so doing it is advisable, from the historic point of view, to discuss a few phases of the old alkaloidal classification, at the same time calling attention to the fallacies found in each statement, which in most cases consist in the fact that while the statement is true for alkaloids it also applies to other substances no longer considered alkaloids.

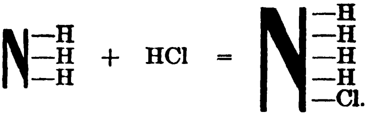
I. "Alkaloids are basic, turning red litmus paper blue, and combining with acids to form salts." True, but so do other bodies, such as methylamine (p. 638) and aniline (p. 779).

II. "Alkaloids are nitrogen bases, and are built on the ammonia type." True, but so are such compounds as mono-, di-, and tri-methylamine, and tetramethyl ammonium iodide (p. 638).

Before leaving this subject, however, it is well to employ it in order to explain why the formula of any alkaloidal salt is the formula of the alkaloid from which derived, plus the formula of the acid, *including its hydrogen.* Thus the formula of morphine hydrochloride, is $C_{17}H_{19}NO_3HCl$, while the formula of morphine, is $C_{17}H_{19}NO_3$.

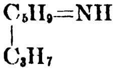
We have already learned (p. 501) the formation of a salt from ammonia was different from the formation of a sodium, potassium, or any other metallic salt, the reaction being graphically:

$NH_3 + HCl = NH_4Cl$



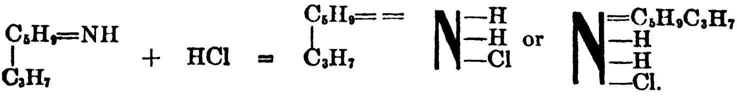
$$N\begin{cases}-H\\-H\\-H\end{cases} + HCl = N\begin{cases}-H\\-H\\-H\\-H\\-Cl.\end{cases}$$

On this ammonia type are the alkaloids built, one, two, or all the hydrogen atoms being replaced by complex organic radicles; thus, one of the simplest, coniine, is—



$$\begin{array}{l}C_5H_9{=}NH\\ |\\ C_3H_7\end{array}$$

and just as $NH_3 + HCl = NH_4Cl$, as shown above, so does coniine plus hydrochloric acid combine as follows:



$$\begin{array}{l}C_5H_9{=}NH\\ |\\ C_3H_7\end{array} + HCl = \begin{array}{l}C_5H_9{=}{=}\\ |\\ C_3H_7\end{array} N\begin{cases}-H\\-H\\-Cl\end{cases} \text{ or } N\begin{cases}=C_5H_9C_3H_7\\-H\\-H\\-Cl.\end{cases}$$

Even so does the valence of the nitrogen in morphine change from III to V in the conversion of the free alkaloid into the salt. This also explains why the salt is named morphine hydrochloride (hydrochlorate, U.S.P. 1890), and not morphine chloride.

III. "There are a special line of reagents producing precipitates with alkaloids. Such alkaloidal precipitants are Mayer's reagent (potassio-mercuric iodide), gold chloride, tannic acid, silicotungstic acid, etc." True, but these same reagents precipitate almost any amido derivative.

IV. "Alkaloids are grouped into the amines (liquid alkaloids) and the amides (solid alkaloids)." By amines we mean those bodies having the general formula RNH_2 (p. 638), while amides are those bodies having the general formula $RCONH_2$—that is, where the hydroxyl of the carboxyl group is replaced by the NH_2 group. The statement that the solid alkaloids are amides is not wholly true, as the solid alkaloids, atropine, cocaine, and morphine, do not contain the $RCONH_3$ group.

Alkaloids are either solid or liquid, the greater number of them being solid. Among the liquid alkaloids that might be mentioned are nicotine, coniine, and lobeline. No fixed rule can be given as to the difference in the structure between the solid and the liquid alkaloids; the general statement that the liquid alkaloids are free from oxygen is not always true. Thus, the liquid alkaloid pelletierine contains oxygen.

Alkaloids usually occur in the form of salts, the most abundant natural alkaloidal combinations being citrates, malates, and tannates. The alkaloids found in cinchona are generally salts of quinic acid, while the alkaloids of opium are usually combined in the drug with meconic acid. So far, very few alkaloids have been found in monocotyledonous plants, the only two of importance derived from plants of that order being colchicine and veratrine, the greater majority of the alkaloids being found in the plants of the dicotyledonous series, although curious to relate, two of the most important families of this group, the two containing the largest number of species, namely, the natural orders Compositæ and Labiatæ, contain no alkaloids. On the other hand, with some plant families, such as the Solanaceæ and Papaveraceæ, almost every represented species contains alkaloids.

As to nomenclature, note that the Pharmacopœia reserves the termination "ine" for alkaloids only, using "in" for glucosides and neutral principles. Other countries do not make this distinction, terminating the names of all active principles of drugs with "in." For comparison, let us tabulate the pharmacopœial Latin and English names of a typical glucoside and a typical alkaloid:

	LATIN	ENGLISH
GLUCOSIDE, U.S.P.	Salic*inum*.	Salic*in*.
ALKALOID, U.S.P.	Quin*ina*.	Quin*ine*.
ALKALOID, U.S.P. 1870	Quinia.	

The last termination has still considerable hold in the Southern States, where there are frequent calls for "sulfate of cinchonidia" (now cinchonidina in Latin, and cinchonidine in English) or for "quinia sulfas."

EXTRACTION OF ALKALOIDS

On no subject in pharmacy does there seem to be less information of recent character, than there is as far as the commercial extraction of alkaloids is concerned. This is partly due to the diversity of methods that may be employed for each drug; as well as the fact that modern alkaloidal plants keep their processes secret. So it is that while an outline of extraction is given under each alkaloid discussed on the pages which follow most of these methods are those published by earlier writers.

In attempting to give a general outline of the way that alkaloids are obtained, it may be said that the drug is first extracted with acidulated water or alcohol. If the latter menstruum is used, the alcohol is distilled off and the residue taken up with acid, and this acidulated aqueous liquid is made alkaline with potassa, soda, ammonia, or milk of lime—thereby liberating the alkaloid which precipitates from solution. The freed alkaloid is either collected on a filter and purified by recrystallization from the appropriate solvent or more generally while still in the liquid is "shaken out" (p. 162) with a solvent immiscible in water—say gasoline, petroleum ether, chloroform, or ether. The freed alkaloid dissolves in this solvent, the solution separated from the now exhausted aqueous layer, the solvents evaporated off, and the crude alkaloid purified by recrystallization, usually as a salt rather than as the free alkaloid. Of course, the bare outline omits the details of purification employed in each case, these details being taken up in discussing the individual drugs.

Lloyd has shown that most alkaloids are adsorbed by hydrous aluminum silicate (see p. 549). Such adsorbed alkaloids are now marketed under the name *alcresta* preparations.

CLASSIFICATION OF ALKALOIDS

Pyridine derivatives:

- Piperidine.
- Piperine.
- Coniine.
- Pilocarpine, U.S.P.
- Pelletierine, U.S.P.
- Nicotine.
- Sparteine.

Tropine derivatives:
- Tropine.
- Atropine, U.S.P.
- Homatropine, U.S.P.
- Scopolamine, U.S.P.
- Hyoscine.
- Hyoscyamine, U.S.P. X.
- Cocaine, U.S.P.
- Beta-eucaine, U.S.P.
- Procaine, U.S.P.

Quinoline derivatives:
- Quinine, U.S.P.
- Quinine Ethylcarbonate, U.S.P.
- Quinidine, U.S.P.
- Cinchonine.
- Cinchonidine, N.F.
- Strychnine, U.S.P.
- Veratrine, U.S.P. IX.

Isoquinoline derivatives:
- Isoquinoline.
- Papaverine, N.F.
- Narcotine.
- Cotarnine, N.F.
- Hydrastine.
- Hydrastinine.
- Emetine, U.S.P.

Phenanthrene derivatives:
- Morphine, U.S.P.
- Diacetyl-morphine.
- Ethyl-morphine, U.S.P.
- Apomorphine, U.S.P.
- Codeine, U.S.P.

Unallotted and special:
- Physostigmine, U.S.P.
- Aconitine, U.S.P. X.
- Colchicine, U.S.P.
- Ephedrine.
- Arecoline, N.F.

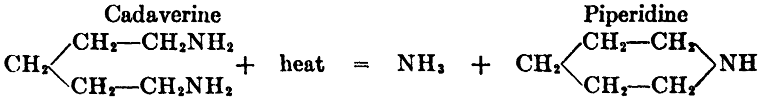
The other alkaloids such as *gelsemine*, *cissampeline*, etc., are but little understood.

Note.—In the table just given, alkaloids bearing the initials "U.S.P." are official either as free alkaloid or as a salt. In other words it does not necessarily mean that the free alkaloid is official, nor that none of its salts is official.

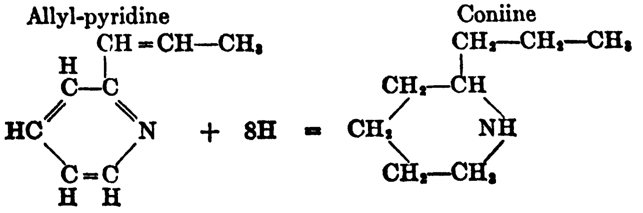
GROUP I.—THE PYRIDINE DERIVATIVES

The chemistry of pyridine has already been considered on p. 898. Its hydrogen compound, *hexahydropyridine*, $C_5H_{11}N$, is called *piperidine*, and was discovered by Rochleder in 1849 on heating piperine with soda lime.

Piperidine is obtained from *cadaverine* (or *pentamethylene diamine*), a substance found in decaying flesh. On heating this body ammonia is driven off, with the formation of piperidine, as shown below:



Piperidine is here mentioned not because of its value in pharmacy, but because its propyl derivative is an alkaloid of importance by reason of being the first alkaloid made synthetically. This alkaloid is coniine. *Coniine* was isolated by Giesecke in 1827 from the fruit of *Conium maculatum*. It is alpha-propyl-piperidine, and its synthesis was accomplished by Ladenberg in 1886 by reduction of allyl-pyridine:

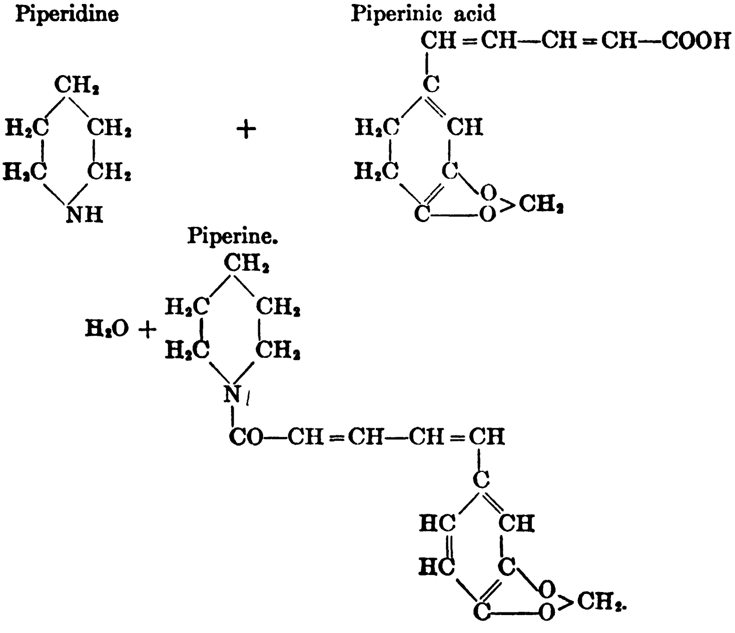


Synthetic coniine is identical with the natural product obtained from conium, except that it is optically inactive, while the natural coniine is dextrogyrate. As already mentioned on p. 684, when an inactive form of an optically active chemical is known, it usually consists of equal quantities of the dextrogyrate and the levogyrate forms of this substance. Following this theory, the inactive synthetic coniine must be a mixture of the dextrogyrate and the levogyre alkaloid. Now, if the natural coniine is the dextrogyre, while the artificial is a mixture of the dextrogyre with levogyre, it follows that if levogyre is removed, the dextrogyre will remain and, by reason of this theory an effort was made to remove the levogyrate form from the synthetic inactive product by special crystallizations, and a product exactly identical with the natural was obtained.

As mentioned above, coniine is the alkaloid found in *Conium maculatum,* and is rarely used in medicine.

Piperina (U.S.P. VIII), or *Piperine,* is a feebly basic substance obtained from pepper. In preparing it, powdered pepper is boiled for fifteen minutes with milk of lime. The mixture is evaporated to dryness on a water bath and the piperine is extracted from the residue with ether. The crude piperine is then recrystallized from alcohol.

Piperine is the combination of piperidine with piperinic acid, and has been made synthetically from these substances, viz.:

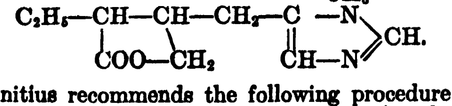


Likewise, when treated with alcoholic potassa, piperine splits into piperidine and piperinic acid.

As piperine does not readily form salts with acids, some authorities no longer consider it an alkaloid, U.S.P. VIII seeming to hold to that opinion by defining it as "a feebly basic substance."

Piperine is a useful antiperiodic, given in 3-Gm. doses.

Pilocarpine.—*Composition.*—The formula of pilocarpine is supposed to be—



$$C_2H_5\text{—}\underset{\text{COO—}}{CH}\text{—}\underset{\text{CH}_2}{CH}\text{—}CH_2\text{—}\underset{\text{CH—N}}{C}\text{—}\overset{CH_3}{N}\!>\!CH.$$

Extraction.—Chemnitius recommends the following procedure. Extract 500 Gm. of pilocarpus with 80 per cent alcohol and 1.5 per cent of carbon tetrachloride in a suitable hot-extraction apparatus. Distil the alcohol from the percolate and add water to the residue and then "shake out" the mixture with melted paraffin (p. 1020). After the paraffin has become solidified to a cake, remove same, wash it with water and mix the washings with aqueous alkaloidal solution mentioned above. Make this solution alkaline with 10 per cent sodium hydroxide solution, shake out with chloroform, separate the chloroformic solution and recover the solvent by distillation. The residue, consisting of the crude pilocarpine, is converted into the nitrate and this is purified by recrystallization.

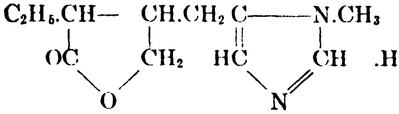
The "shaking out" with chloroform will be explained on page 1020. The following salts of pilocarpine are official.

Pilocarpinæ Hydrochloridum (U.S.P. X; N.F. VI), or *Pilocarpine Hydrochloride*, has been relegated to the Formulary. The salts of pilocarpine, like the drug pilocarpus, are valuable sudorifics and sialogogues. *Dose.*—By mouth, 5 mg. (1/12 grain).

PILOCARPINÆ NITRAS—Pilocarpine Nitrate

(Pilocarpin. Nitras)

$C_{11}H_{16}O_2N_2.HNO_3$



Molecular weight, 271.16

The nitrate of an alkaloid obtained from the dried leaflets of *Pilocarpus Jaborandi* Holmes, or of *Pilocarpus microphyllus* Stapf (Fam. *Rutaceæ*).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

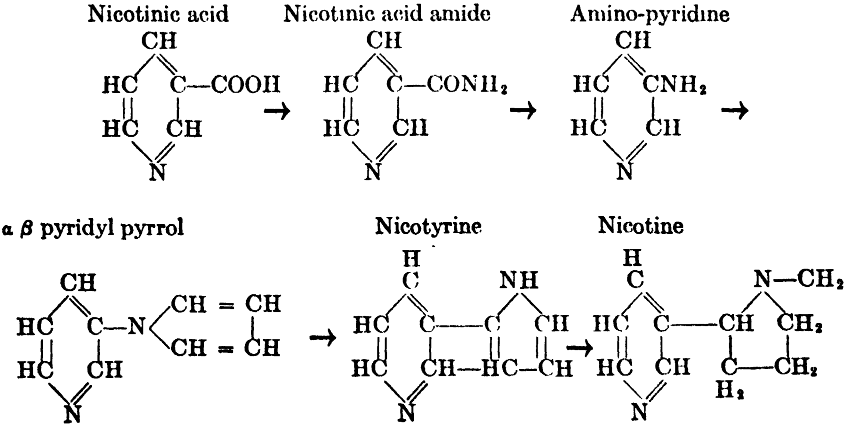
Shining crystals; soluble in about 4 parts of water; and in about 60 parts of alcohol; insoluble in chloroform and ether; melts between 170° and 173° C. For details, see U.S.P., p. 290.

For *tests for identity* and for *impurities* (chloride, carbonizable matter, other alkaloids), see U.S.P., p. 290.

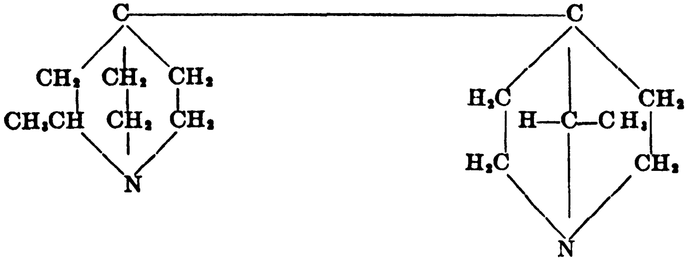
Medical Properties.—Used just like the hydrochloride.

Dose.—See the hydrochloride.

Nicotine.—Nicotine was isolated from tobacco by Posselt in 1828. Investigations show that this alkaloid is piperidyl-tetrahydro-methyl-pyrrol, the graphic formula of which is given below. The structural formula was worked out by Pictet and Crepieux in 1895, whose work, however, did not lead to the synthesis of the alkaloid, but only as far as nicotyrine, the derivative of nicotine shown in the graphic formulas given below:



Sparteine.—The structural formula of this alkaloid is supposed to be:



Sparteina Sulfas (N.F. VI), or *Sparteine Sulfate*, is the sulfate of an alkaloid obtained from *Cytisus Scoparius*. It is extracted from this plant by treating it with acidulated water, the liquid is then made alkaline with sodium hydroxide, and from this alkaline liquid the alkaloid, which is volatile, is separated by distillation. It is purified by dissolving in diluted hydrochloric acid, evaporating to dryness, and the alkaloid freed by treatment with potassium hydroxide is redistilled. The salts are made from the alkaloid by treatment with the appropriate acid. The sulfate occurs in colorless hygroscopic crystals which are soluble in 1.1 parts of water and 2.4 parts of alcohol. It is used as a diuretic in ½-grain doses.

GROUP II.—THE TROPINE DERIVATIVES

The very important alkaloids of the nightshade families are derivatives of tropine, this being an artificial alkaloid which is a decomposition product of atropine, and since its structure is similar to that substance from which it is derived, chemists consider it as the base upon which atropine is built.

The synthesis starts with a substance containing a ring of seven carbon atoms, *cycloheptene* (Fig. 1). From this the dimethyl-amido combination (Fig. 2) is prepared and this with hydrochloric acid and subsequent distillation yields *tropidine* (Fig. 3), which on treatment with caustic alkalis yields tropine (Fig. 4).

Fig. 1.

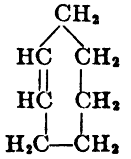


Fig. 2.

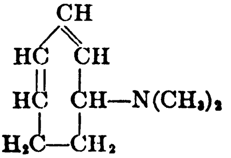


Fig. 3.

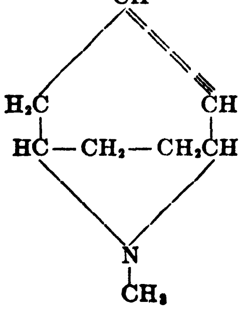
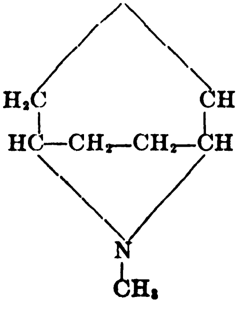


Fig. 4.



It will be seen that this synthesis starts with a ring of seven carbon atoms and by introduction of one amido group becomes a pyridine ring with a chain of two carbon atoms extending from pyridine carbon atom 3 to carbon atom 5 (Fig. 5). At present a more compact formula is however used. Thus tropine is presented as in Fig. 6.

Fig. 5.

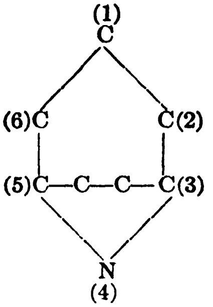
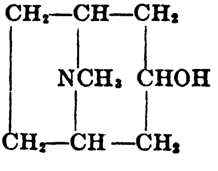
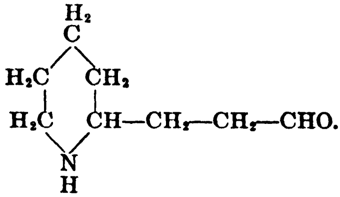


Fig. 6.



Pelletierine, $C_8H_{15}NO$, is supposed to have the following structural formula:



Extraction.—See under pelletierine tannate.

PELLETIERINÆ TANNAS—Pelletierine Tannate

(Pellet. Tann.)

A mixture of the tannates of the several alkaloids obtained from pomegranate, *Punica Granatum* Linné (Fam. *Granataceæ*).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Light yellow, odorless, amorphous powder; astringent taste; soluble in about 250 parts of water and in about 12.6 parts of alcohol; less soluble in ether; insoluble in chloroform. For details, see U.S.P., p. 278.

For *tests for identity* and for *impurities* (foreign alkaloids), see U.S.P., p. 278.

Manufacture.—Ground pomegranate bark is mixed with milk of lime and extracted with water. The percolate is shaken with chloroform and the separated chloroformic layer is shaken with diluted sulfuric acid. The acid solution of the sulfates of the alkaloids is treated with tannic acid and the precipitated tannates collected on a filter and dried.

Remarks.—As mentioned in the official definition given above, this body is a mixture of alkaloids each of which resembles the tropines in structure. The structural formula of the chief constituent of the mixture, pelletierine, is given above.

The free alkaloidal mixture is a volatile liquid, but the official tannate, like all salts of liquid alkaloids, is a solid.

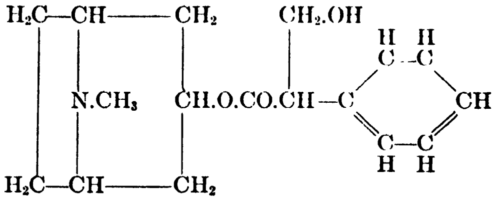
Medical Properties.—Teniafuge.

Dose.—250 mg. (4 grains).

ATROPINA—Atropine

(Atrop.)

$C_{17}H_{23}O_3N$



Molecular weight, 289.19

An alkaloid usually obtained from belladonna.

Storage.—Preserve in well-closed containers.

Summarized Description.

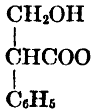
White crystals; extremely poisonous; soluble in about 455 parts of water and in about 1.5 parts of alcohol; also soluble in glycerin, chloroform and ether; melts between 114° and 116° C.; optically inactive. For details, see U.S.P., p. 77.

Color Test.—Vitali's reaction. See U.S.P., p. 77 and also below.

For *tests for identity* and for *impurities* (carbonizable matter, foreign alkaloids, apoatropine and belladonnine), see U.S.P., p. 77.

Extraction.—The alcoholic percolate from belladonna is made alkaline by treatment with milk of lime and then filtered. The filtrate (a solution of free alkaloid) is acidulated with diluted sulfuric acid, freed from fat and resin by evaporation of the alcohol, and taking up with acidulated water. The acidulated aqueous filtrate is then treated with alkali, and the free alkaloid thus precipitated is washed with water, dissolved in alcohol, and crystallized from this solution of addition by a little water. Duilius mixes the powdered drug with sodium hydroxide solution and sodium carbonate and extracts the dry powder with ether. The solvent is recovered by distillation, the alkaloidal residue is dissolved in 5 per cent acetic or sulfuric acid and from this solution the atropine and hyoscyamine are precipitated by addition of ammonia water. The precipitated alkaloids are then purified.

Remarks.—Atropine is a tropine tropate, and can be made by treating tropine with tropic acid in the presence of hydrochloric acid.

Tropic acid is phenyl-hydracrylic acid,  $\begin{array}{l} CH_2OH \\ | \\ CHCOOH \\ | \\ C_6H_5 \end{array}$, and when it is combined with tropine, the product of the union—atropine—is assumed to have the formula given above.

Vitali's reaction for atropine is interesting. When the alkaloid is treated with fuming nitric acid and evaporated to dryness, and a drop of potassium hydroxide be added to the dry residue, it will give a violet-blue color, and if the residue is again covered with alcohol, the isonitril odor (p. 646), is evolved. The color reaction part of Vitali's test is given in the present Pharmacopœia.

Atropine is a sedative and mydriatic.

Incompatibilities.—See prescription No. 77 in Chapter LIX.

Dose.—$\frac{4}{10}$ mg. ($\frac{1}{150}$ grain).

ATROPINÆ SULFAS—Atropine Sulfate

(Atrop. Sulf.)

$(C_{17}H_{23}O_3N)_2.H_2SO_4.H_2O$ Molecular weight, 694.47

Storage.—Preserve in well-closed containers.

Summarized Description.

White crystalline efflorescent powder; very poisonous; soluble in about 0.4 part of water, in about 4 parts of alcohol and in about 3.1 parts of glycerin; less soluble in chloroform; sparingly soluble in ether, responds to the barium chloride reaction for sulfates. For details, see U.S.P., p. 77.

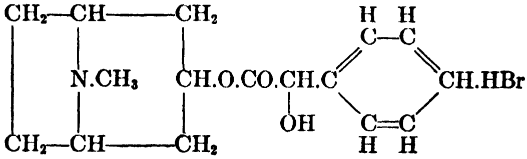
For *other tests* and for *impurities*, see atropine.

Remarks.—Atropine sulfate, being more soluble than the uncombined alkaloid, is generally used instead of the latter.

Dose.—4/10 mg. (1/150 grain).

HOMATROPINÆ HYDROBROMIDUM—Homatropine Hydrobromide

(Homatrop. Hydrobrom.)



$C_{16}H_{21}O_3N.HBr$ Molecular weight, 356.10

Summarized Description.

White, odorless, crystalline powder or white crystals; very poisonous; solutions dilate the pupil of the eye; soluble in about 6 parts of water, in about 32 parts of alcohol and in about 630 parts of chloroform. For details, see U.S.P., p. 185.

For *tests for identity* and for *impurities* (foreign alkaloids, atropine, hyoscyamine and scopolamine), see U.S.P., p. 185.

Remarks.—Homatropine is an artificial alkaloid made by the condensation of tropine and mandelic acid. It is phenyl-glycocoll-tropin.

Its action is similar to atropine, but is less poisonous. As a mydriatic —a dilator of the pupil of the eye—it is preferable to atropine, because it works more rapidly.

Dose.—1/2 mg. (1/120 grain).

Hyoscyamine.—Hyoscyamine, as the formula $C_{17}H_{23}NO_3$ shows, is isomeric with atropine, and when atropine or hyoscyamine is treated with weak baryta water, each split into tropic acid and tropine. When it is said that hyoscyamine and atropine are isomeric, it must not be understood that the two are identical, for we have already learned, when considering tartaric acids (p. 684), that there may be many chemicals having similar formula, but different characteristics.

Amenomiya has shown that atropine (which is optically inactive) consists of the official hyoscyamine (which is levogyre) and a dextrogyrate alkaloid isomeric with hyoscyamine.

Extraction.—Hyoscyamine is extracted either from the mother liquor left after atropine crystallization or from hyoscyamus seeds freed from fat by percolation with petroleum ether. The fat-free seeds are extracted with 85 per cent alcohol acidulated with hydrochloric acid, the alcohol evaporated from percolate in vacuo, and the watery residue again treated with petroleum ether or chloroform to remove fat and color. The liquid is then made alkaline with potassium carbonate and shaken out with chloroform. The chloroformic solution is then evaporated at low temperature, and the crude alkaloid that remains is purified by crystallization from diluted sulfuric acid solution. From this crystalline sulfate the alkaloid can be obtained by making its aqueous solution alkaline, shaking out with chloroform, and evaporating the chloroformic solution.

Hyoscyaminæ Hydrobromidum (U.S.P. X), or *Hyoscyamine Hydrobromide*, was recognized in the former Pharmacopœias. It has a therapeutic effect similar to atropine and is administered in 1/100-grain doses.

Hyoscyaminæ Sulfas (U.S.P. VIII), or *Hyoscyamine Sulfate*, $(C_{17}H_{23}NO_3)_2H_2SO_4$, is used the same as the hydrobromide and in the same dose.

Hyoscine.—This alkaloid has the formula $C_{17}H_{21}NO_4$, and is isomeric with scopolamine (see below). Some time since there was much controversy relative to the composition of hyoscine, some authorities claiming it was isomeric with atropine and hyoscyamine. The present Pharmacopœia takes the view that it is the same as scopolamine and therefore includes the formerly official *hyoscine hydrobromide* in the monograph on scopolamine hydrobromide.

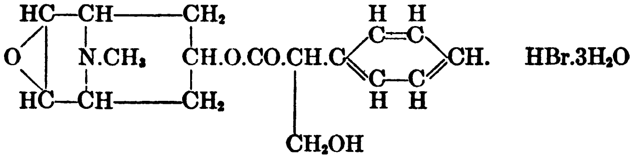
Scopolamine is thought to have the graphic formula given below.

Hyoscine is made from the mother liquor remaining after removal of hyoscyamine from the seed of hyoscyamus or stramonium, by treating the liquor with hydrobromic acid, and crystallizing the resultant hydrobromide.

The crude salt is purified by formation of the double chloride of the alkaloid and gold, and eventual separation of the gold by use of hydrogen sulfide.

SCOPOLAMINÆ HYDROBROMIDUM—Scopolamine Hydrobromide

(Scopol. Hydrobrom.—Hyoscine Hydrobromide)



$C_{17}H_{21}O_4N.HBr.3H_2O$. Molecular weight, 438.14

The hydrobromide of levorotatory scopolamine obtained from plants of the *Solanaceæ.*

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless transparent slightly efflorescent rhombic crystals, very poisonous; soluble in about 1.5 parts of water and in about 16 parts of alcohol; slightly soluble in chloroform; insoluble in ether; when dried it melts between 190° and 192° C.; optical rotation, −22 degrees to −25.75 degrees in a 100-mm. tube. For details, see U.S.P., p. 329.

For *tests for identity* and for *impurities* (foreign alkaloids, apoatropine, morphine), see U.S.P., p. 329.

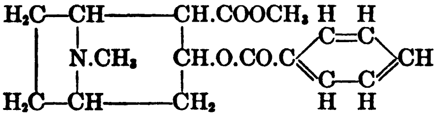
Uses.—Similar to hyoscyamine.

Dose.—5/10 mg. (1/120 grain).

COCAINA—Cocaine

(Cocain.)

$C_{17}H_{21}O_4N$



Molecular weight, 303.17

An alkaloid obtained from the leaves of *Erythroxylon Coca* Lamarck and other species of *Erythroxylon* (Fam. *Erythroxylaceæ*).

Summarized Description.

Large colorless crystals, or white crystalline powder; soluble in about 600 parts of water and in about 5 parts of alcohol; also soluble in chloroform, ether, olive oil and liquid petrolatum; melts between 96° and 98° C.; acid solutions, levorotatory. For details, see U.S.P., p. 123.

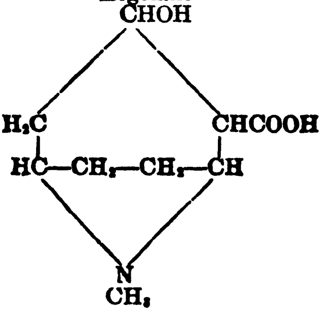
For *tests for identity* and for *impurities*, see cocaine hydrochloride.

Extraction.—Coca leaves are extracted with 0.5 per cent sulfuric acid, the percolate concentrated, made alkaline with sodium carbonate, and shaken out with kerosene. The kerosene solution is shaken with acidulated water, alkaloid precipitated from the aqueous liquid by addition of sodium carbonate is shaken with ether, and the freed alkaloid obtained by evaporation of the ethereal solution is purified by again dissolving in acidulated water, precipitation with alkali, and recrystallization from alcohol or ether.

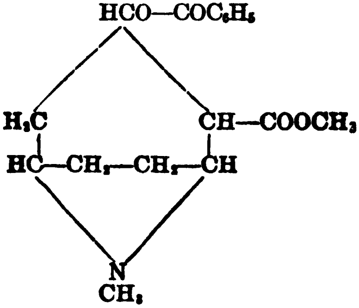
Duilius moistens coca leaves with sodium carbonate solution, dries them, and then extracts the alkaloid with ether or benzene. After distillation of the solvent, the crude alkaloid undergoes suitable purification.

Remarks.—This important alkaloid, which was first isolated from coca leaves by Niemann is now known to be benzoyl-methyl-ecgonine, the ecgonine being a carbonic acid derivative of tropine. A comparison of the formulas of the two substances, ecgonine and cocaine, is given below:

Ecgonine



Cocaine



It has recently been synthesized upon a commercial scale, although the synthetic product does not seem to be upon the market.

Incompatibilities.—See prescriptions Nos. 36 and 94 in Chapter LIX.

Dose.—15 mg. (¼ grain).

COCAINÆ HYDROCHLORIDUM—Cocaine Hydrochloride

(Cocain. Hydrochlor.—Cocaini hydrochloridum P.I.)

$C_{17}H_{21}O_4N.HCl$ Molecular weight, 339.64

Summarized Description.

Colorless crystals, or flaky lustrous leaflets, or white crystalline powder; soluble in about 0.4 part of water in about 2.6 parts of alcohol and in about 18.5 parts of chloroform; also soluble in glycerin; insoluble in ether; levorotatory; melts at not less than 183° C. For details, see U.S.P., p. 124.

For *tests for identity* and for *impurities* (carbonizable substances, cinnamyl-cocaine, isatropyl-cocaine), see U.S.P., p. 124.

Remarks.—This soluble salt of cocaine is the one generally used whenever cocaine is indicated.

Sterilized cocaine solutions are now in some demand. These can be made by heating a 2 to 4 per cent solution between 110° and 120° C., provided the glass vessel employed does not contain free alkali.

It is stated that an alkaline solution of cocaine (*p*H 8.4; see p. 1034) is a more efficient anesthetic than is a neutral or an acid solution.

While cocaine was isolated as far back as 1855, the use of the alkaloid dates from the last fifty years, a demand for the product not being started until local anesthetic action of cocaine had become known in 1884. When small quantities of cocaine are rubbed on the mucous membrane or injected beneath the skin, a benumbing of the nerves in that immediate neighborhood results, and so thorough is this insensibility that operations can be performed without pain where great agony would be produced were the parts not cocainized. On account of this valuable action of cocaine its use in all minor surgical operations spread widely, particularly in dentistry and operations on the nose and throat. From its original legitimate purpose cocaine has been prostituted into producing a sedative action in cases where wholly unnecessary. This is particularly true of catarrh powders, and it is through the use of such catarrh powders containing cocaine that the abuse of the drug increased throughout the country, until it became necessary to pass a rigid national law preventing its use except upon physicians' prescriptions.

Dose.—15 mg. (¼ grain).

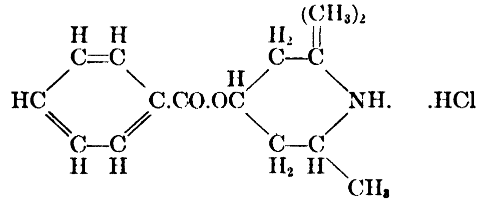
COCAINE SUBSTITUTES

Since the pernicious effects of cocaine have become known, efforts have been made to prepare local anesthetics devoid of habit-forming properties, or at least, not so dangerous in that direction. A number of these, three official, are described below. Several of the latest types of cocaine substitutes are based upon the assumption of Macht (p. 797) that the local anesthetic action of cocaine rests in its benzyl group.

EUCAINÆ HYDROCHLORIDUM—Eucaine Hydrochloride

(**Eucain. Hydrochlor.**—Beta-eucaine Hydrochloride)

$C_{15}H_{21}O_2N.HCl$



Molecular weight, 283.64

Eucaine Hydrochloride, when dried to constant weight at 100° C., contains not less than 99 per cent of $C_{15}H_{21}O_2N.HCl$.

Storage.—Preserve in well-closed containers.

Summarized Description.

White crystalline powder; soluble in about 30 parts of water, in about 28 parts of alcohol and in about 9 parts of chloroform. For details, see U.S.P., p. 150.

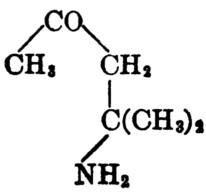
For *tests for identity* and for *impurities* (carbonizable substances, cocaine, alpha-eucaine), see U.S.P., p. 150.

For *assay*, see U.S.P., p. 150.

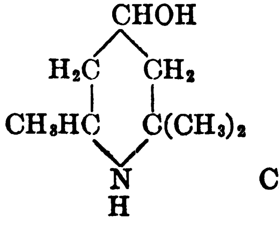
Remarks.—This official is a synthetic alkaloid, the hydrochloride of trimethyl-benzoyl-hydroxypiperidine.

It is made by treating diacetonamine (*a*) with paraldehyde, the product reduced by use of metallic sodium to vinyl-di-acetone-alkamine (*b*) and this treated with benzoyl chloride, whereupon the free base eucaine (*c*) results.

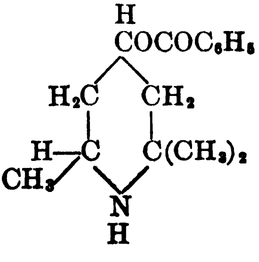
(*a*)
Diacetonamine



(*b*)
Vinyl-di-acetone-alkamine



(*c*)
β-eucaine



It will be seen that eucaine has no chemical connection with cocaine, but, being used like it, is considered at this place. It is claimed that eucaine is an efficient local anesthetic, and that it does not produce a debasing habit, as does cocaine. Eucaine possesses the advantage over cocaine that it is stable and its solutions can be boiled, thus permitting sterilization. Cocaine when heated to the temperature of sterilization is apt to decompose.

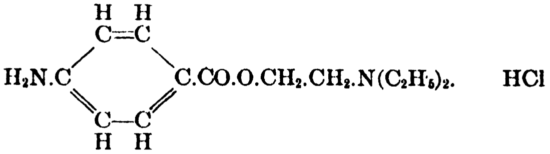
Dose.—Used only externally as local anesthetic.

Borocaine, or *Beta-eucaine Borate,* is recommended by Copeland as a highly efficient anesthetic.

Alpha-eucaine, the hydrochloride of benzoyl-methyl-tetra-methyl-oxypiperidine carboxylic-methyl-ester is used like beta-eucaine.

PROCAINÆ HYDROCHLORIDUM—Procaine Hydrochloride

(Procain. Hydrochlor.—Procaine)



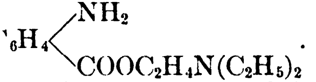
$C_{13}H_{20}O_2N_2.HCl$ Molecular weight, 272.64

Para-aminobenzoyl-diethylaminoethanol hydrochloride.

Summarized Description.

Small colorless crystals or white crystalline powder; soluble in about 0.6 part of water and in about 24 parts of alcohol; sparingly soluble in chloroform and ether; melts between 153° and 156° C. For details, see U.S.P., p. 306.

For *tests for identity* and for *impurities* (phenacaine, cocaine, carbonizable substances, heavy metals), see U.S.P., p. 306.

Remarks.—Procaine, or *novocain,* is para-amino-benzoyl diethylaminoethanol chloride;  $C_6H_4\begin{cases}NH_2\\COOC_2H_4N(C_2H_5)_2\end{cases}$. It occurs in colorless crystals and is a local anesthetic that is much less toxic than cocaine.

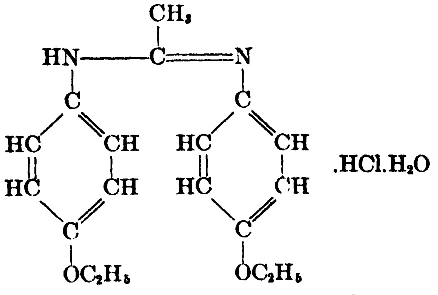
Dose.—Used only externally or hypodermically as a local anesthetic.

Aethylis Aminobenzoas (U.S.P.), or *Benzocaine,* has already been described on p. 797.

PHENACAINÆ HYDROCHLORIDUM—Phenacaine Hydrochloride

(Phenacain. Hydrochlor.)

$C_{18}H_{22}N_2O_2.HCl.H_2O$



Molecular weight, 352.67

The hydrochloride of ethenyl-*p*-diethoxydiphenylamidine.

Storage.—Preserve in well-closed containers.

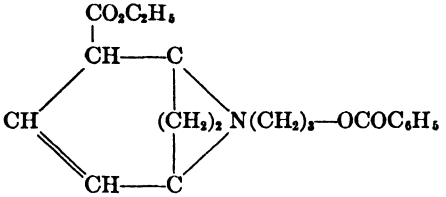
Summarized Description.

Small colorless crystals, permanent in air; odorless; bitter taste producing numbness; soluble in 50 parts of water; freely soluble in alcohol and chloroform; insoluble in ether. For details, see U.S.P., p. 282.

For *tests for identity* and for *impurity* (acetphenetidin) see U.S.P. p. 282.

Remarks.—Phenacaine or *holocaine,* is ethenyl paradiethoxydiphenylamidine chloride. It is made by condensation of paraphenetidin (p. 783) with acetphenetidin. It is used in 1 per cent solution as a local anesthetic.

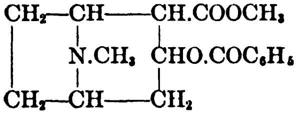
Eckaine is benzoylhydroxypropylnorecgonidine ester.



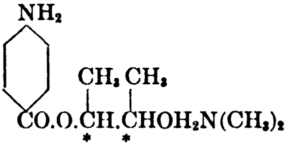
It is a crystalline base, giving a water-soluble chloride and is a powerful local anesthetic.

Among the other modern cocaine substitutes may be cited *psicaine, tutocaine, percaine, pantocaine,* and *larocaine,* the graphic formulæ of which are printed below.

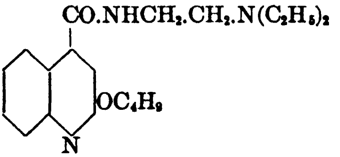
Psicaine.



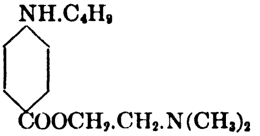
Tutocaine.



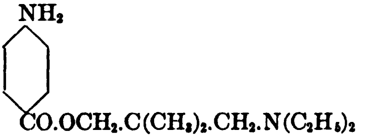
Percaine.



Pantocaine.



Larocaine.

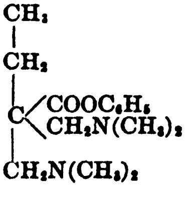


Butyn (N.N.R.) and **Butesin** (N.N.R.) are discussed on pages 797 and 798.

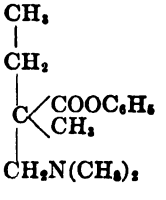
Alypin (N.N.R.) is the hydrochloride of *benzoxy-dimethylamino-methyl-dimethylaminobutane* (formula given below). It is a white crystalline powder, that is very soluble in water. It is employed as a local anesthetic, usually in 2 to 4 per cent solutions.

Stovaine is the hydrochloride of *benzoyl-dimethylamino-ethyl-propanol* (formula given below). It occurs in small brilliant scales melting at 175° C. and is very soluble in water. It is used like alypin.

Alypin.



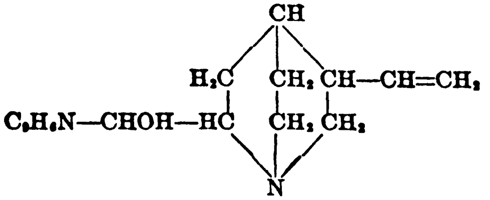
Stovaine.



GROUP III.—QUINOLINE DERIVATIVES

Quinoline itself has already been discussed on page 898, where the structural formula is fully explained, and here reference need only be made to the alkaloidal derivatives of this base.

Cinchonine ($C_9H_6N—C_9H_{12}OH.NCH_3$) is one of the four important alkaloids obtained from the cinchona bark. Of the species of cinchona yielding more or less of this alkaloid, it is found most abundantly in Huanuco cinchona. The structure of cinchonine has been studied from the decomposition products, and is supposed to be—



the quinoline base being attached to a complex piperidine derivative.

Cinchonidine (p. 921) is isomeric with cinchonine and is supposed to have the same structure. Cinchonidine, however, is levogyrate, while cinchonine is dextrogyrate. Quinidine is methoxycinchonine; while quinine is methoxycinchonidine.

Cinchonine Sulfas (N.F. VI) occurs in white lustrous prismatic crystals having a very bitter taste.

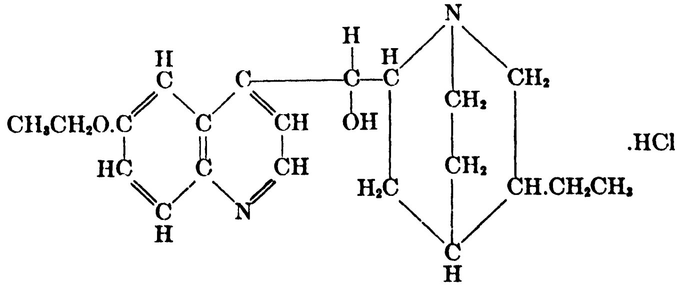
Of the reactions for cinchonine, the only one calling for special attention is the interesting fact that, differing from quinine and cinchonine, it does not give a blue fluorescence in acid solutions. Cinchonine is used as an antipyretic—to reduce fevers—and as a remedy for malaria.

Dose.—150 mg. (2½ grains).

Cupreine, $C_{19}H_{33}N_2O_2$, is hydroxycinchonine and can be considered as demethylated quinine. It is obtained from cuprea bark, *Remija pedunculata*, and is quite abundant but is of little value as a therapeutic agent. Cupreine derivatives, however, are now being employed with considerable success. Among these may be mentioned *optochin* or ethylhydrocupreine, used by intravenous injection in pneumonia, measles and scarlet fever; *vuzin* or iso-octylhydrocupreine, which is active against diphtheria bacilli; *eucuprin,* or iso-amylhydrocupreine, with action similar to optochin.

ÆTHYLHYDROCUPREINÆ HYDROCHLORIDUM—Ethylhydrocupreine Hydrochloride

(Æthylhydrocup. Hydrochlor.)



$C_{21}H_{28}O_2N_2.HCl$ Molecular weight, 376.70

Ethylhydrocupreine Hydrochloride contains, when dried for twenty-four hours over sulfuric acid, not less than 90 per cent of ethylhydrocupreine base ($C_{19}H_{22}N_2OH.O.C_2H_5$).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

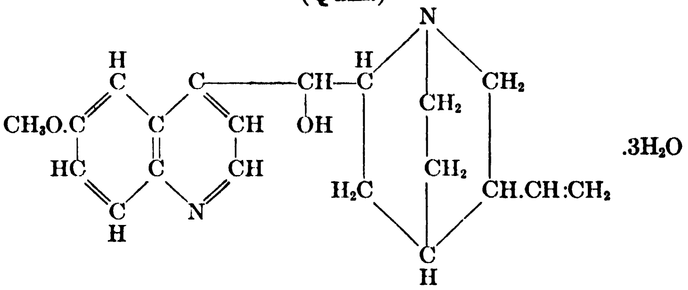
White or yellowish-white powder; odorless and tasteless crystalline, soluble in 2 parts of water, in about 4 parts of alcohol and about 3.7 parts of chloroform; insoluble in ether and petroleum benzin. For details, see U.S.P., p. 40.

For *tests for identity* and for *impurities* (cupreine, ammonium salts, quinine salts and carbonizable substances), see U.S.P., p. 40.

Remarks.—This new official is called *optochin.* It is used intravenously in pneumonia, measles, and scarlet fever. Its chief use is in eye troubles. No dose is given in U.S.P. XI.

QUININA—Quinine

(Quin.)



$C_{20}H_{24}O_2N_2.3H_2O$ Molecular weight, 378.25

An alkaloid obtained from cinchona.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White, microcrystalline, efflorescent powder; slowly developing, but intense and persistent bitter taste; soluble in about 1560 parts of water and in about 0.6 part of alcohol; also soluble in chloroform and ether; sparingly soluble in ammonia water; alcohol solution is levorotatory; solution in diluted sulfuric acid is intensely fluorescent. For details, see U.S.P., p. 313.

For *tests for identity* and for *impurities* (carbonizable substances, ammonium salts, other cinchona alkaloids), see U.S.P., p. 313.

Extraction.—There are so many old methods of extraction of the cinchona alkaloids found in the literature and so little modern information on the subject, that the following process, given by Field, is offered merely as a type. The bark is mixed with about one fifth of its weight of slaked lime and is then extracted with a mixture of 75 per cent of kerosene and 25 per cent of fusel oil. The percolate is then shaken out with 6 per cent sulfuric acid; the acid layer is separated, neutralized with saturated solution of sodium hydroxide and decolorized with animal charcoal, after which it is filtered into lead-lined crystallizing boxes. After twelve hours the separated crystals are removed from the mother liquid by use of a filter press. This first crop of crystals (chiefly quinine sulfate with some cinchonidine sulfate) are recrystallized until a pure quinine salt is obtained. To the mother liquor mentioned above, sodium carbonate solution is added and the separating alkaloids are dissolved in diluted acid and are recrystallized. The purified alkaloidal mixture is then treated with enough tartaric acid to make a normal tartrate and as a result the tartrates of quinine and cinchonidine are precipitated. To the "tartrated" mother liquor, containing quinidine and cinchonine, enough tartaric acid is added to make acid tartrates, which precipitate from boiling solutions. This crystalline precipitate is treated with concentrated sulfuric acid, which dissolves the quinidine; the residue is then treated with the kerosene-fusel oil mixture, which dissolves the remaining quinine and cinchonidine; after which the still undissolved cinchonine is crystallized from diluted sulfuric acid. In other methods, gasoline is used as the extracting solvent; the quinidine is removed by use of ammonia and the cinchonidine is precipitated by addition of a solution of Rochelle salt.

Remarks.—This important alkaloid was isolated by Pelletier and Caventou, two apothecaries of Paris, in 1820. Investigations show that quinine is a methoxycinchonidine, $C_9H_5(OCH_3)N—CHOH—C_9H_{14}N$.

The synthesis of quinine has not yet been accomplished.

Of the reactions given in the Pharmacopœia quite characteristic is the blue fluorescence produced when quinine is dissolved in acid. A very beautiful test is the thalleioquin test; which, as given in the Pharmacopœia, consists of the treatment of a faintly acid quinine solution with bromine water, and the excess of ammonia, when the liquid assumes a vivid green tint.

Another characteristic test is the one based on the production of *herapathite,* the green crystals of quinine iodosulfate formed when the alkaloid is mixed with acetic acid, alcohol and sulfuric acid and is then treated with an alcoholic solution of iodine.

Besides, in the free form, quinine is recognized by the Pharmacopœia as bisulfate, dihydrochloride, ethyl-carbonate, sulfate, and the hydrochloride with urea. The National Formulary also recognizes the hydrobromide, hydrochloride, phosphate, and the salicylate. Of these salts of quinine the most popular is the sulfate. Quinine sulfate is only sparingly soluble in water, but when an aqueous mixture of the sulfate is treated with sulfuric acid, the salt rapidly goes into solution. This is due to the formation of the bisulfate of quinine, one part of which dissolves in 9 parts of water, whereas 1 part of quinine sulfate requires 810 parts of water for solution. There is a question, however, as to the wisdom of dispensing quinine solutions, as by dissolving the salt its bitter taste is made still more pronounced. It is, in fact, preferable to administer the same in a mixture with a "shake well" label, and in such a mixture the taste of the quinine can be effectively masked by the use of preparations of licorice, such as ammoniated glycyrrhizin or an aqueous fluidextract of licorice (such as in now official). Compound syrup of sarsaparilla has also been found useful to mask the taste of quinine, but it is not so effective as are licorice preparations.

There has been a great demand for the preparations of quinine devoid of the disagreeable taste. For adults the administration of quinine capsules covers the need, but in the case of children who cannot swallow capsules some liquid method of administration is exceedingly desirable. The new official, quinine ethyl carbonate, has the tremendous advantage of being almost tasteless and quinine tannate has also but little bitterness. The nearest approach to a palatable quinine liquid is a licorice combination of quinine, as cited above. In fact, practically the only way satisfactorily to administer quinine internally to children is as quinine tannate in the form of chocolate lozenges, and this method is highly satisfactory. The physiologic effect of quinine can also be secured by preparing an ointment of quinine (the alkaloid or the sulfate) with benzoinated lard or petrolatum and hydrous wool-fat, this ointment being applied by rubbing under the armpits. Oleate of quinine, N.F. V, can be used for the same purpose.

Physicians at times prescribed quinine with licorice, then direct addition of diluted sulfuric acid to dissolve the quinine. In such combination (see p. 1059) the sulfuric acid will immediately precipitate the glycyrrhizin from the licorice preparation, producing an unsightly mixture, and at the same time one which is nauseatingly bitter.

The writer knew of one physician who prescribed the sulfate under the name of "Sulfat de Pelletiere," the object of this peculiar synonym being the same as actuated the physician who prescribed the same substance under the name of "Sulfatis Americanis Australis" (South American sulfate). In each case the patient had a notion that quinine was repugnant to her system, and in order to permit the administering of same without arousing her suspicions, these peculiar synonyms were employed. It must be said, however, that the first synonym is scarcely short of dangerous, inasmuch as the alkaloid pelletierine, obtained from pomegranate bark (see p. 907), is an article of commerce, and now official as the tannate, and "Sulfat de Pelletiere" should be left to designate the sulfate of this alkaloid.

It has been stated that when quinine is dispensed in solution along with organic acids (acetylsalicylic acid, etc.) it is converted into a poisonous isomere *quinotoxine*. Sollmann thinks that the danger of such a change has been exaggerated.

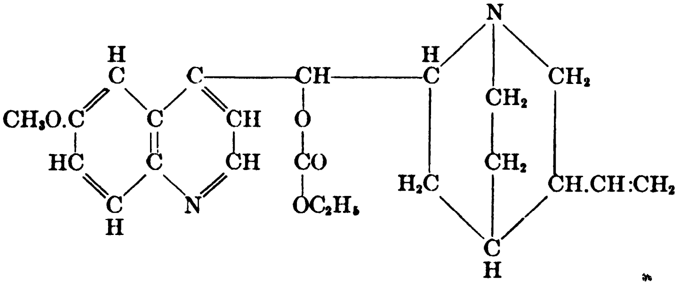
Incompatibilities.—See prescriptions Nos. 7, 25, 27, 33, 41, 60, and 61 in Chapter LIX.

In view of the full description of quinine and its salts just given, it is now necessary merely to insert the Pharmacopœia data relative to the official salts of quinine.

Dose.—As antimalarial at least 1 Gm. (15 grains) daily.

QUININÆ ÆTHYLCARBONAS—Quinine Ethylcarbonate

(Quin. Æthylcarb.—Euquinine)



$C_{23}H_{28}O_4N_2$ Molecular weight, 396.23

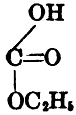
Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Fine white soft needles, usually matted into fleecy masses; odorless; not bitter until chewed; darkens on exposure to light; slightly soluble in water; soluble in about 1.7 parts of alcohol, in about 1.5 parts of chloroform and in about 7.2 parts of ether; readily soluble in dilute acids, such solutions being fluorescent; melts between 89° and 91° C. For details, see U.S.P., p. 314.

For *tests for identity* and for *impurities* (chloride and sulfate), see U.S.P., p. 314.

Remarks.—This official derivative of quinine was originally introduced under the name, *euquinine.* It is the quinine ester of ethyl-carbonic acid:



$$\begin{array}{l} OH \\ C{=}O \\ OC_2H_5 \end{array}$$

the hydrogen of the hydroxyl group being replaced by the quinine group, $(C_{20}H_{23}N_2O)^1$. It occurs in a fleecy conglomeration of delicate white needles that are practically tasteless. This absence of taste explains the popularity of *euquinine.*

Dose.—See Quinine.

QUININÆ BISULFAS—Quinine Bisulfate

(Quin. Bisulf.—Quinine Acid Sulfate)

$C_{20}H_{24}O_2N_2.H_2SO_4.7H_2O$ Molecular weight, 548.39

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, transparent, efflorescent orthorhombic crystals or small needles; very bitter taste; turns yellow on exposure to light; soluble in about 9 parts of water, in about 18 parts of alcohol and in about 18 parts of glycerin; sparingly soluble in chloroform and ether. For details, see U.S.P., p. 315.

For *tests for identity* and for *impurities*, see quinine sulfate.

Dose.—See Quinine.

QUININÆ ET UREÆ HYDROCHLORIDUM—Quinine and Urea Hydrochloride

(Quin. et. Urea Hydrochlor.)

$C_{20}H_{24}O_2N_2.HCl.CO(NH_2)_2.HCl.5H_2O$ Molecular weight, 547.26

Quinine and Urea Hydrochloride contains not less than 58 per cent and not more than 65 per cent of anhydrous quinine [$C_{20}H_{24}O_4N_2$].

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, translucent prisms or white granular powder; very bitter taste; soluble in about 0.9 parts of water and in about 2 parts of alcohol. For details, see U.S.P., p. 316.

For *tests for identity* and for *impurities* (carbonizable matter and ammonium salts), see Quinine.

Outline of Assay.—Make aqueous solution alkaline with ammonia water and then shake out with three portions of chloroform. Chloroformic extract on evaporation is dried and weighed. Yield at least 58 per cent of weight of original sample. For details, see U.S.P., p. 316.

Remarks.—This quinine derivative, which is sometimes called *chininum bihydrochloricum carbamidum*, is made by making a solution of quinine dihydrochloride and then adding to this the molecular quantity of urea. It has lately attained great popularity not merely as an ideal quinine salt for hypodermic administration, but as a local anesthetic.

Dose.—Hypodermic (one dose daily), 1 Gm. (15 grains).

QUININÆ DIHYDROCHLORIDUM—Quinine Dihydrochloride

(Quin. Dihydrochlor.)

$C_{20}H_{24}O_2N_2.2HCl$ Molecular weight, 397.13

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White powder; very bitter taste; soluble in about 0.6 part of water and in about 10 parts of alcohol; slightly soluble in chloroform and in ether. For details, see U.S.P., p. 316.

For *tests for identity*, see U.S.P. For *impurities* (carbonizable substances, sulfate, barium, other cinchona alkaloids), see U.S.P., p. 316.

Remarks.—This salt of quinine has the same advantage over the hydrochloride that the bisulfate has over the sulfate; superior solubility. Thus while the hydrochloride requires 16 parts of water to effect solution, the dihydrochloride is soluble in 0.6 part of water. Like all quinine salts, it is a tonic and antimalarial.

Dose.—See Quinine.

QUININÆ SULFAS—Quinine Sulfate

(Quin. Sulf.)

$(C_{20}H_{24}O_2N_2)_2.H_2SO_4.2H_2O$ Molecular weight, 782.51

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White, silky, light, flexible, glistening, efflorescent crystals, making an easily compressible mass, or hard prismatic monoclinic needles; persistent bitter taste; darkens on exposure to light; soluble in about 810 parts of water, in about 86 parts of alcohol and in about 36 parts of glycerin; slightly soluble in chloroform and ether; easily soluble in a mixture of 2 volumes of chloroform and 1 volume of dehydrated alcohol; solution in diluted sulfuric acid shows vivid blue fluorescence. For details, see U.S.P., p. 317.

For *tests for identity* (including thalleioquin reaction), see U.S.P., p. 317.

For *impurities* (inorganic salts, carbonizable substances, other cinchona alkaloids), see U.S.P., p. 317.

Remarks.—The official test for distinguishing quinine from other cinchona alkaloids is a modification of *Kerner's test*, which required that when a mixture of the quinine salt and water is macerated and then filtered, the filtrate should yield a clear liquid with a specific quantity of ammonia water.

Quinine and all its alkaloids are valuable antipyretics and antiperiodics, that is, they reduce fever and relieve malaria. The different acids combined with the alkaloid in the several salts somewhat modify the action according to the properties of the acid.

Dose.—See Quinine.

Quininæ Tannas (U.S.P. X), or *Quinine Tannate*, is a mixture of quinine with tannic acid, containing between 30 and 35 per cent of the alkaloid. It is useful because it is almost devoid of bitterness. It is admirably adapted for making chocolate lozenges of quinine for administration to children.

Quinine Hydrobromide, Quinine Hydrochloride, Quinine Phosphate and **Quinine Salicylate** are recognized by the National Formulary. The student should consult the N.F. monographs on these several salts.

Quinidine.—*Extraction.*—See Quinine (p. 916).

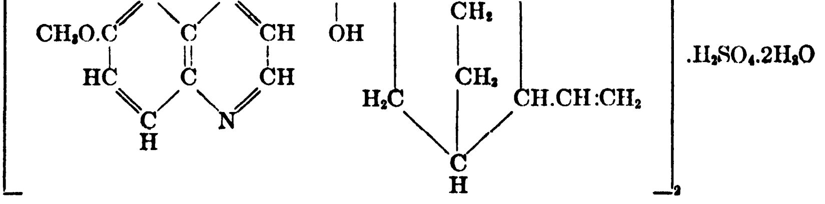
Remarks.—Quinidine, $C_{20}H_{24}N_2O_2$, is isomeric with quinine, and, like it, is supposed to be methoxycinchonine.

The salts of quinidine, like those of quinine, show a fluorescence in acid solution, and quinidine also responds to the thalleioquin test.

U.S.P. XI recognizes the sulphate of this alkaloid.

QUINIDINÆ SULFAS—Quinidine Sulfate

(Quinidin. Sulf.)



$(C_{20}H_{24}O_2N_2)_2.H_2SO_4.2H_2O$ Molecular weight, 782.51

The sulfate of an alkaloid obtained from cinchona.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Fine acicular crystals frequently cohering in masses; very bitter taste; darkens on exposure to light; soluble in about 90 parts of water and about 8 parts of alcohol; soluble in chloroform but almost insoluble in ether; dextrorotary; acid solutions show vivid blue fluorescence. For details, see U.S.P., p. 312.

For *tests for identity* and for *impurities* (other alkaloids, carbonizable substances, ammonium and other inorganic salts, other cinchona alkaloids), see U.S.P., p. 313.

Remarks.—This salt of quinidine was official in the Pharmacopœia of 1890 and was omitted from U.S.P. VIII and U.S.P. IX. It now comes back into U.S.P. XI, since medical studies of the past decade have shown its great value in the treatment of cases involving irregularity of heart action. Quinidine sometimes produces unpleasant and even dangerous effects, such as nausea, vomiting and even convulsions.

Dose.—200 mg. (3 grains). It should be used with caution.

Quinidine and other cinchona alkaloids combined with oleic acid in solution in petroleum distillates are now used by spraying as effective moth preventatives.

Cinchonidine.—*Extraction.*—See Quinine (p. 916).

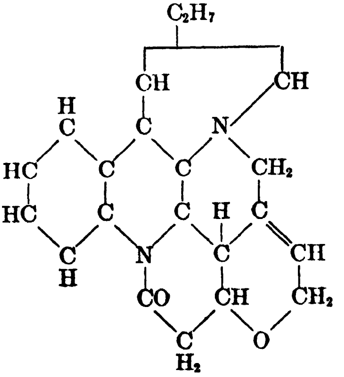
Remarks.—Cinchonidine is isomeric with cinchonine, and is supposed to have the same graphic formula (p. 915). It is only sparingly soluble in ammonia water, and this explains the principle of Kerner's test for quinine described on page 920.

A striking test for cinchonidine is the color produced by the oxidation of the alkaloid by means of a crystal of potassium dichromate and sulfuric acid, when a brilliant, grass-green color results.

Cinchonidinæ Sulfas (U.S.P. X; N.F. VI), or *Cinchonidine Sulfate*, enjoyed a large sale prior to 1880, when the high price of quinine sulfate (which then sold at $5 an ounce), made that important alkaloid a luxury. It is used like quinine, but is not so effective. *Dose.*—150 mg. (2½ grains).

Strychnine (U.S.P. IX) was discovered by Pelletier and Caventou in 1818. It is the active principle of nux vomica and Ignatia bean, from which it is extracted as explained below.

Robinson, after years of research, inclines to the belief that the graphic formula of strychnine is



The configuration of the 2 atoms of carbon and the 7 atoms of hydrogen given at the top of the formula has not, as yet, been worked out.

Extraction.—Nux vomica is extracted with a diluted alcohol containing a trace of sulfuric acid. To the tincture thus obtained is added slaked lime enough to neutralize the acid after which the alcoholic solution of the free alkaloid is filtered from the lime precipitate and the alcohol is distilled. The residue after distillation of the alcohol is dissolved in diluted acid and to the filtrate enough ammonia is added to precipitate the strychnine and the brucine. The latter is then dissolved from the mixture by the use of cold diluted alcohol. Then the residue is treated with boiling alcohol, which dissolves the strychnine, and this is decolorized by treatment with animal charcoal. The alkaloid is eventually precipitated from the alcoholic solution by treatment with alkali.

The synthesis of strychnine has not yet been accomplished. Interesting among the reactions of strychnine is its behavior under different oxidizing agents. Thus, when strychnine is first dissolved in concentrated sulfuric acid (which it does without any change in color), and when a small crystal of potassium dichromate is added, a violet color changing to tints of red, then orange, and yellow results. This test is said to detect 1 part of strychnine in 500,000. Its accuracy is however questioned, Professor J. U. Lloyd having shown that a mixture of morphine and hydrastine will give a similar color reaction. Professor Lloyd makes the confusion of such a combination for strychnine a dramatic feature of one of his romances.

Strychnine is a potent poison, producing symptoms akin to tetanus. Among the antidotes that have been suggested are morphine, chloral, chloroform, magnesium sulfate (25 per cent solution of intraspinal injection) or sodium amytal in 12-grain doses.

A very prominent characteristic of strychnine is its intensely bitter taste, the bitterness being shown in a dilution of 1 to 200,000. Ward and Munch find eriodictyon preparations the best masker of its bitterness.

Incompatibilities.—See prescriptions 33 and 77 in Chapter LIX.

It is recognized by the Pharmacopœia in the form of the nitrate and the sulfate. The phosphate is recognized by the National Formulary.

STRYCHNINÆ NITRAS—Strychnine Nitrate

(Strych. Nitras)

$C_{21}H_{22}O_2N_2.HNO_3$ Molecular weight, 397.20

The nitrate of an alkaloid obtained chiefly from nux vomica.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, glistening needles or white, crystalline powder; bitter, very poisonous; soluble in about 45 parts of water, in about 120 parts of alcohol and in about 65 parts of glycerin; less soluble in chloroform; insoluble in ether; aqueous solution is levorotatory. For details, see U.S.P., p. 362.

Color Tests.—Blue, then violet, then purple-red and lastly orange or yellow with sulfuric acid and potassium dichromate.

For other *tests for identity* and for *impurities* (carbonizable substances, brucine, chloride, sulfate), see U.S.P., p. 362.

Remarks.—This official compound, like the other salts of strychnine, is a powerful nervous stimulant.

Dose.—2 mg. ($\frac{1}{30}$ grain).

STRYCHNINÆ SULFAS—Strychnine Sulfate

(Strych. Sulf.)

$(C_{21}H_{22}O_2N_2)_2.H_2SO_4.5H_2O$ Molecular weight, 856.53

The sulfate of an alkaloid obtained chiefly from nux vomica.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless or white, efflorescent, prismatic crystals or white, crystalline powder; soluble in about 35 parts of water and in about 65 parts of alcohol; also soluble in glycerin, less so in chloroform; insoluble in ether. For details, see U.S.P., p. 363.

Color Tests.—See Strychnine Nitrate. Also purple then cherry-red color with ammonium vanadate and sulfuric acid.

For *other tests for identity* and for *impurities* (carbonizable substances, brucine), see U.S.P., p. 363.

Remarks.—This is the most popular of the strychnine salts and like the others it is used as a nervous stimulant.

Dose.—2 mg. ($\frac{1}{30}$ grain).

Brucine is an unofficial alkaloid, associated with strychnine in nux vomica and ignatia. It is of little importance in pharmacy and medicine, except that some commercial strychnine has not been fully purified from brucine. This is detected by the fact that brucine when treated with concentrated nitric acid gives a brilliant red tint, while strychnine will dissolve practically colorless.

Brucinæ Sulfas (N.F. VI), or *Brucine Sulfate,* is a constituent of a veterinary preparation, *liquor nucis vomicæ alkaloidorum* (p. 214).

Veratrina (U.S.P. IX; N.F. V), or *Veratrine,* is a mixture of alkaloids obtained from the seed of *Asagræa officinalis.* It is a gray-white extremely poisonous powder and in its manufacture powdered cevadilla seeds are extracted with 90 per cent alcohol, the percolate concentrated and poured into a large quantity of water, thus precipitating resin, fat, etc. The aqueous liquid is then made alkaline with ammonia, and the precipitated veratrine purified by washing with water, dissolving in diluted hydrochloric acid, and precipitating with ammonia.

The word veratrine, as applied to this alkaloid, is unfortunate, inasmuch as it would suggest that the alkaloid is obtained from the official veratrum. This is not the case, the alkaloid having originally been discovered in cevadilla seeds in 1818, by Meissner, who called the alkaloid sabadilline, suggesting, however, that if the same alkaloid was found in other species of veratrum, it might be well to call it veratrine. The same year, however, Pelletier and Caventou isolated veratrine from white veratrum, and from this fact the alkaloid obtained its name.

The chemistry of this alkaloid has been comparatively little studied. As above mentioned, it is now considered a mixture of alkaloids. It is a quinoline derivative, as shown by its decomposition products.

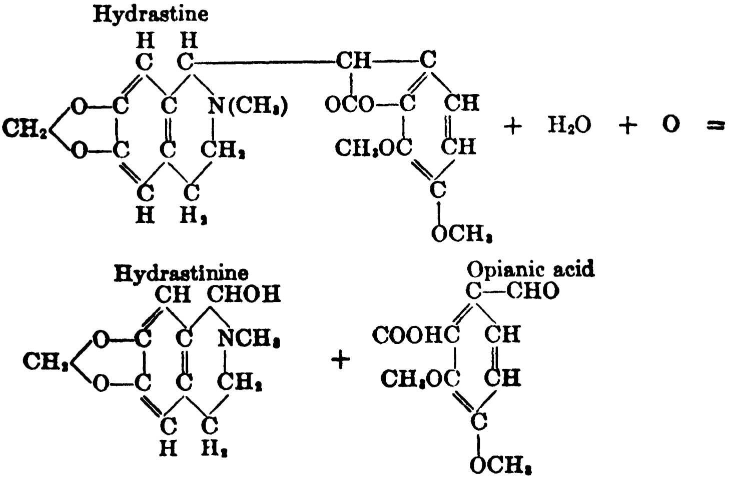
Its chief reactions are the colors produced with concentrated sulfuric acid, the tint ranging from yellow to cherry red, according to conditions of mixing.

Veratrine is used internally very seldom, and then as a sedative. Its chief use is externally as a destroyer of vermin and in some forms of skin trouble, in which case it is usually dispensed as *oleate of veratrine* (N.F. V) or as the *ointment* (N.F. V).

Group IV.—The Isoquinoline Derivatives

Isoquinoline is a substance having the same empiric formula as quinoline, the only difference between the two being in the location of the nitrogen atom. (See formula of quinoline on p. 898.)

Hydrastine (U.S.P. IX) is an alkaloid obtained from golden seal. Upon treatment with oxidizing agents (diluted nitric acid), it splits into hydrastinine and opianic acid:



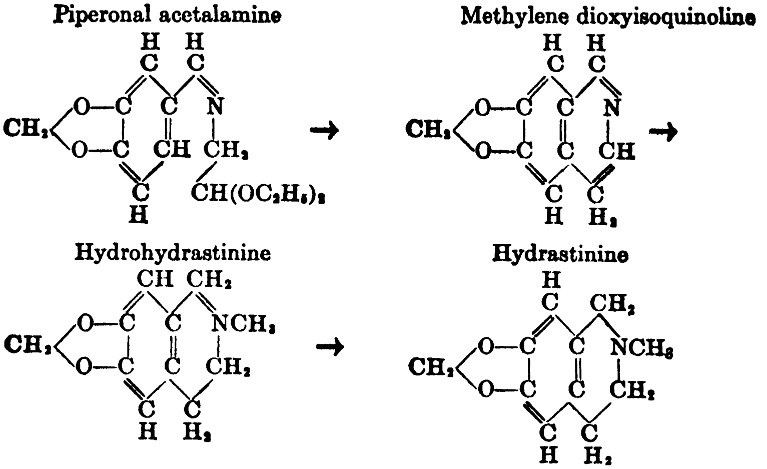
It is extracted by first preparing an acetic decoction of hydrastis. This is evaporated to a syrup and mixed with three volumes of 20 per cent sulfuric acid. This causes the separation of the crystals of bisulfate of berberine (yellow hydrastine). The mother liquor is made alkaline with ammonia, and the crude precipitated hydrastine is purified by recrystallization with alcohol or acetic acid.

Hydrastine occurs in handsome white crystals, soluble in 135 parts of alcohol and insoluble in water. It is largely used as an astringent, and especially in gonorrheal washes. Unfortunately, two articles are known in commerce as hydrastine, the white crystals above described, which are quite expensive, and the so-called *yellow hydrastine* which is nothing less than berberine. *Dose.*—10 mg. (⅙ grain).

Hydrastinæ Hydrochloridum (N.F. VI), or *Hydrastine Hydrochloride,* is a water-soluble salt of the alkaloid. It is a constituent of *compound solution of hydrastinine* (N.F. V).

Berberine is an unofficial alkaloid obtained from hydrastis and also from the root of *Berberis vulgaris*; hence its name. To these drugs it transmits its characteristic yellow color. Its structural formula is similar to hydrastine and to the alkaloids of calumba (see p. 879) although even more complex.

Hydrastinine.—This is an artificial alkaloid obtained from hydrastine by treatment with appropriate oxidizing agents. The synthesis of hydrastinine from piperonal acetalamine has been accomplished, the successive stages of this synthesis being graphically shown below:

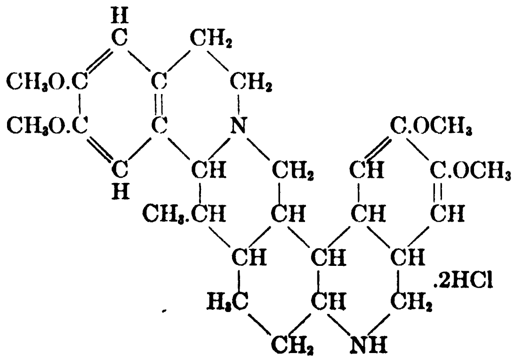


Hydrastininæ Hydrochloridum (U.S.P. IX), or *Hydrastinine Hydrochloride,* was recognized in a former Pharmacopœia as a water-soluble compound of hydrastinine. Its aqueous solutions possess a blue fluorescence resembling that of quinine solutions. It is used as a uterine astringent in 30-mg. doses.

Papaverine, Narcotine and **Cotarnine** are isoquinoline compounds. They will be discussed among the opium alkaloids (p. 929).

EMETINÆ HYDROCHLORIDUM—Emetine Hydrochloride

(Emet. Hydrochlor.)



$C_{29}H_{40}O_4N_2.2HCl$ Molecular weight, 553.26

The hydrochloride of an alkaloid obtained from ipecac or prepared synthetically.

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

White or slightly yellow crystalline powder, darkening on exposure to light; freely soluble in water or alcohol; does not lose more than 16 per cent of its original weight at 100° C. For details, see U.S.P., p. 139.

Color Test.—Bright green with sulfuric acid-molybdic acid reagent.

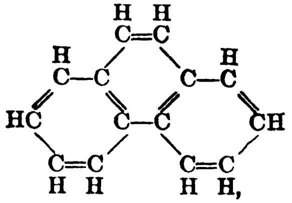
For other *tests for identity* and for *impurities* (carbonizable substances, cephaëline), see U.S.P., p. 139.

Remarks.—This isoquinoline derivative has the graphic formula which is given above. During the last twenty years, it has come into vogue as a remedy for amebic dysentery and for pyorrhea.

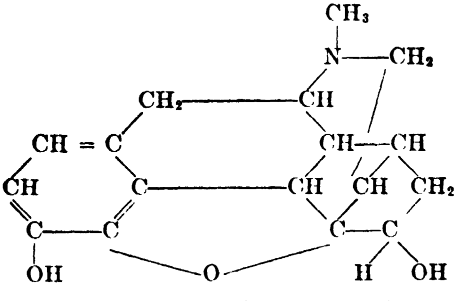
Dose.—60 mg. (1 grain) daily by parenteral injection.

GROUP V.—PHENANTHRENE DERIVATIVES

The difficulty of making a clear-cut definition for alkaloids is shown in the case of morphine and its allied opium alkaloids. The definition for alkaloids, given on p. 900, states that they are derivatives of pyridine, quinoline, or allied bodies, and yet latest investigations seem to show that morphine, one of the most prominent alkaloids, is not a derivative of isoquinoline as long supposed, but is derived from phenanthrene, an isomere of anthracene, with its nitrogen atom not in the main ring but in a side "morphinoline" ring. The graphic formula of phenanthrene is—



and the graphic formula of morphine is supposed to be



Morphina (U.S.P. IX) is, with the possible exception of quinine, the most important of the alkaloids. It is also interesting as being the first alkaloid to be isolated, its separation from opium being accomplished by Sertürner, an apothecary of Eimbeck, in 1806.

It is extracted by preparing an aqueous infusion of opium which is then made alkaline and the precipitated alkaloid after filtration and washing, is dissolved in a diluted sulfuric acid. This acid solution is decolorized by filtration through animal charcoal, is then concentrated and is crystallized in a leaden tank. If the solution is of the proper density when it is stirred while cooling, the morphine sulfate crystallizes suddenly to a solid mass. This accomplished, the mother liquor is allowed to drain from the tank, the crystalline mass is cut into bricks, which are placed upon absorbent surfaces and are then allowed to dry. During this drying, the coloring matter comes to the surface of the brick forming a brown or black scurf. This is cut off with a sharp knife, leaving the rest of the brick practically pure morphine sulfate. From this, of course, the other salts of morphine and the alkaloid itself can be prepared.

It is stated that morphine is now being made synthetically upon a commercial scale.

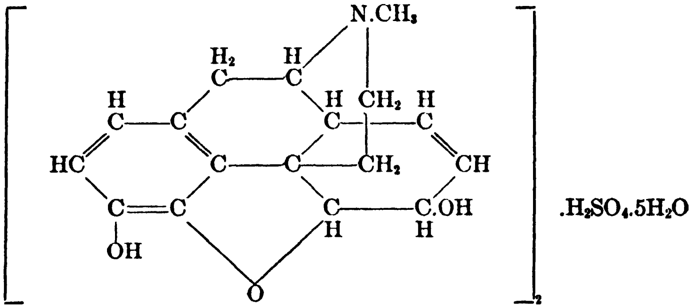
Morphine exhibits a number of interesting color reactions. Among these may be cited the purple then blue color produced with sulfuric and molybdic acids and the blue-green-brown color-play produced by action of morphine on sulfuric acid and selenous acid. These tests distinguish morphine from the other opium alkaloids.

Morphine, when sprinkled upon concentrated nitric acid, gives a red color similar to brucine. The reaction, however, differs from the brucine reaction by being less permanent, and is of value, distinguishing morphine from quinine.

Morphine is used like opium as a hypnotic and sedative.

Morphine is official in the form of the sulfate (U.S.P. XI) and the hydrochloride (N.F. VI).

MORPHINÆ SULFAS—Morphine Sulfate
(Morph. Sulf.)



$(C_{17}H_{19}O_3N)_2.H_2SO_4.5H_2O$ Molecular weight, 758.47

The sulfate of the alkaloid morphine.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White, feathery, acicular, silky crystals or cubical masses or white crystalline powder; soluble in about 15.5 parts of water and in about 460 parts of alcohol; insoluble in chloroform or ether; gives barium chloride test for sulfates. For details, see U.S.P., p. 237.

For *tests for identity* and for *impurities* (codeine, meconate, ammonium salts, foreign alkaloids), see U.S.P., p. 237.

Remarks.—The pharmacopœial formula of morphine is the same as this given above, although the configuration is slightly different.

Magendie's solution is an aqueous solution of morphine sulfate, 16 grains to the fluidounce. *Syrup of Morphine,* 1 grain morphine to the fluidounce, is used in the South, where a mixture of equal quantities of the syrups of squill, tolu, morphine, and ipecac is prescribed as *"four syrups,"* or *"syrupus quattuor."*

Morphine solutions are apt to show growth of molds (*Penicillium glaucum,* etc.) upon standing. A small piece of camphor in such solutions prevents the growth of molds.

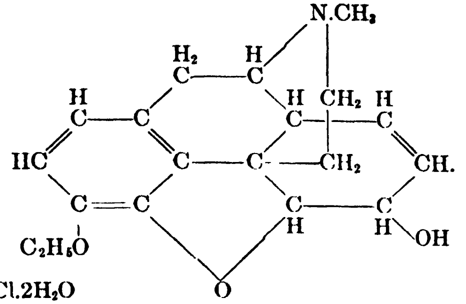
Dose.—8 mg. (1/8 grain).

Morphinæ Hydrochloridum (N.F. VI), or *Morphine Hydrochloride,* was recognized in the U.S.P. during several revisions. *Dose.*—8 mg. (1/8 grain).

Diacetylmorphine (U.S.P. IX), which was introduced under the name *heroin,* is an acetic ester of morphine prepared by replacing two hydroxyl groups of that alkaloid by acetyl groups. This acetylization is accomplished by heating morphine with acetyl chloride, washing the product with diluted alkali solution and then with water and finally crystallizing from alcohol. It is used as a sedative and since it has had an enormous illegitimate use, President Coolidge, on June 7, 1924, signed the Porter Bill, prohibiting the manufacture of this chemical from opium or any derivative thereof.

ÆTHYLMORPHINÆ HYDROCHLORIDUM—Ethylmorphine Hydrochloride

(Æthylmorph. Hydrochlor.)



$HCl.2H_2O$

$C_{19}H_{23}O_3N.HCl.2H_2O$ Molecular weight, 385.68

The hydrochloride of a monoethyl ether of morphine.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

White or yellowish, odorless, microcrystalline powder; soluble in about 8 parts of water and in about 17 parts of alcohol; slightly soluble in chloroform and ether; melts at 123° C., with decomposition. For details, see U.S.P., p. 43.

Color Test.—Green, then violet blue, when warmed with ferric chloride and sulfuric acid. Deep red, when foregoing mixture is treated with nitric acid.

Impurities.—Ammonium compounds, morphine, codeine, see U.S.P., p. 43.

Remarks.—This morphine derivative is largely used under the trade name, *dionin.* It is made by the action of ethyl iodide on morphine in the presence of alkali. It has been claimed to be devoid of the objectionable qualities of morphine.

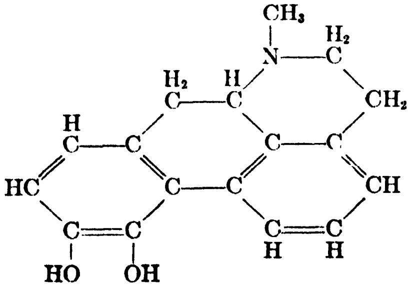
Dose.—15 mg. (¼ grain).

Apomorphine.—This interesting artificial alkaloid is prepared by heating morphine with concentrated hydrochloric acid in sealed tubes to 150° C. The sealed tubes in this case are tubes of glass about a quarter of an inch thick and 3 feet long, originally in the shape of an ordinary test tube. The ingredients are placed in this tube, and then the upper portion is drawn to a fine point by heating in a blast lamp flame. In this way the ingredients are sealed within the walls of glass. This tube is then wrapped up in paper and placed within an iron tube, stoppered at one end with an appropriate cap. This tube is then placed in a suitable oven and is heated for the requisite time, and after cooling for a time the sealed tip is opened cautiously to permit the escape of the compressed gases, and is finally broken by cutting with a glass file.

The formula for apomorphine differs from that of morphine simply by the loss of one molecule of water and the rearrangement of the "morphinoline" ring, which is removed by the action of concentrated hydrochloric acid, as mentioned above.

APOMORPHINÆ HYDROCHLORIDUM—Apomorphine Hydrochloride

(Apomorph. Hydrochlor.)



$.HCl.—H_2O$

$C_{17}H_{17}O_2N.HCl.\frac{1}{2}H_2O$ **Molecular weight, 312.61**

Apomorphine Hydrochloride is the hydrochloride of an alkaloid prepared from morphine.

Storage.—Preserve in small tightly-stoppered vials, which have been previously rinsed with diluted hydrochloric acid and dried. It must be protected from light.

Caution.—Apomorphine hydrochloride must be rejected if it at once imparts an emerald-green color to 100 parts of distilled water when shaken with it in a test tube.

Summarized Description.

Minute white or grayish-white, glistening monoclinic prisms; turns green on exposure to light and air; soluble in about 50 parts of water and about 45 parts of alcohol; slightly soluble in chloroform or ether. For details, see U.S.P., p. 62.

For *tests for identity* and for *impurities* (decomposition products), see U.S.P., p. 62.

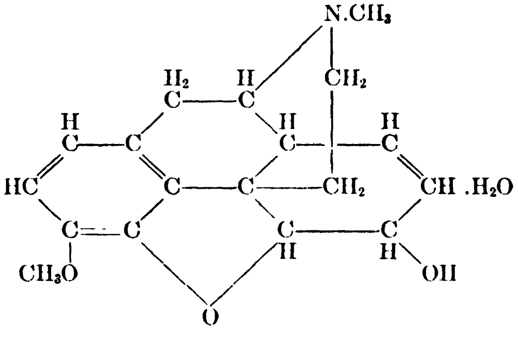
Remarks.—Apomorphine hydrochloride dissolves in water in a colorless solution, but on standing it changes to a greenish tint. The nature of the decomposition is not yet fully understood, but is worth bearing in mind in prescription practice since a green solution should not be dispensed. However, Gorrell and Gray find that the green color of the solution does not affect its pharmacologic action.

This alkaloid salt is emetic, being of particular value employed hypodermically in cases of attempted suicide by poisoning.

Dose.—Expectorant, 1 mg. (1/60 grain); emetic, hypodermic, 5 mg. (1/12 grain).

CODEINA—Codeine

(Codein.)



$C_{18}H_{21}O_3N.H_2O$ Molecular weight, 317.19

An alkaloid obtained from opium or prepared from morphine by methylation.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless, translucent slightly efflorescent crystals or white crystalline powder; soluble in about 120 parts of water and in about 1.6 parts of alcohol; also soluble in chloroform, benzene and ether; aqueous solution is levorotatory; when dried melts between 154° and 156° C.

Color Tests.—Green, then blue, then grass-green, with sulfuric acid-selenous acid reagent. Blue by adding ferric chloride solution to sulfuric acid then red by adding nitric acid. For details, see U.S.P., p. 125.

Impurities (morphine, carbonizable matter), see U.S.P., p. 125.

Extraction.—The aqueous infusion of opium is concentrated and treated with calcium chloride, which holds the alkaloids in solution as hydrochlorides, while the meconic acid, color, etc., are precipitates. The filtrate is concentrated, when the hydrochlorides of codeine and morphine crystallize. The mixed salts are redissolved in water and the solution made alkaline with ammonia, which precipitates the morphine. The filtrate on concentration yields crystals of codeine hydrochloride, and the free alkaloid is obtained from this by treatment with potassa. The above process is also another of the many methods for obtaining morphine from opium.

Remarks.—Codeine is another of the numerous alkaloids found in opium, and can be obtained synthetically by treatment of morphine with potassium hydroxide and methyl iodide. This synthesis and other investigations show that it is methyl ether of morphine.

Characteristic reactions of codeine are, as of many alkaloids already studied, the behavior of the substance with concentrated sulfuric acid and various oxidizing or reducing agents, such as nitric acid, ferric chloride, selenous acid, and formaldehyde. These tests are of value in distinguishing codeine from morphine, as is also the fact that codeine turns yellow with nitric acid and *not* red, as does morphine.

Dose.—30 mg. (½ grain).

CODEINÆ PHOSPHAS—Codeine Phosphate

(Codein. Phos.)

$C_{18}H_{21}O_3N.H_3PO_4.1\frac{1}{2}H_2O$ Molecular weight, 424.24

Codeine Phosphate contains not less than 70 per cent of anhydrous codeine ($C_{18}H_{21}O_3N$).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Fine, white, efflorescent needle-shaped crystals or crystalline powder; soluble in about 2.3 parts of water and in about 261 parts of alcohol; sparingly soluble in chloroform and ether.

For *tests for identity* and for *impurities* (sulfate, chloride, morphine), see U.S.P., p. 126.

Color Tests.—See Codeine.

Outline of Assay.—Dissolve the salt, make the solution alkaline with sodium hydroxide and shake out four times with chloroform. Evaporate the chloroformic extract, dry and perform residual titration with N/10 H_2SO_4 and N/10 NaOH. For details, see U.S.P., p. 126.

Dose.—30 mg. (½ grain).

CODEINÆ SULFAS—Codeine Sulfate

(Codein. Sulf.)

$(C_{18}H_{21}O_3N)_2.H_2SO_4.5H_2O$ Molecular weight, 786.50

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

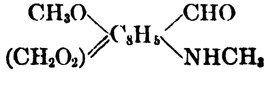
Long, white, glistening, needle-shaped efflorescent crystals, rhombic prisms or crystalline powder; soluble in about 30 parts of water and in about 1035 parts of alcohol, insoluble in chloroform or ether.

For *tests for identity* and for *impurities* (morphine and carbonizable matter), see above and also U.S.P., p. 127.

Remarks.—The uncombined alkaloid, as well as the phosphate and the sulfate, are official, and these are used as sedatives in cough-mixtures and the like, being administered in much larger doses than is morphine and its salts—½ grain being considered as a safe dose of any of three official forms.

Dose.—30 mg. (½ grain).

Cotarninæ Chloridum (U.S.P. X; N.F. VI), or *Cotarnine Chloride*, is the chloride of quaternary oxymethyl-oxymethylene-dihydro-isoquinoline:



$$\begin{matrix} CH_3O \\ (CH_2O_2) \end{matrix} > C_8H_5 < \begin{matrix} CHO \\ NHCH_3 \end{matrix}$$

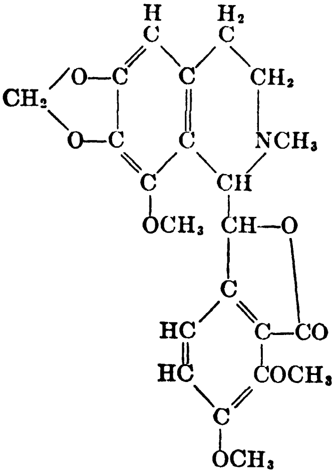
It is made by the hydrolysis of narcotine and has also been produced synthetically from myristicin (p. 854). Its name is a quaint inversion of the word narcotine and it is frequently prescribed under the name *stypticine*. It is used as an analgesic, uterine sedative and hemostatic, although Hanzlik doubts its value for the latter purpose. *Dose.*—60 mg. (1 grain).

Papaverinæ Hydrochloridum (N.F. VI), or *Papaverine Hydrochloride*, is a new addition to the Formulary. This opium alkaloid is an isoquinoline derivative, its formula being given below. The difference between its therapeutic action and that of the other opium alkaloids is due, according to Macht, to the presence of the benzyol group. Papaverine is used as an analgesic, local anesthetic and sedative. It is only slightly toxic.

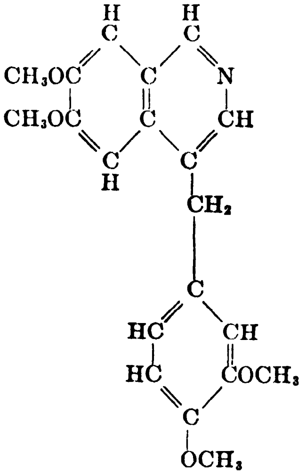
Dose.—60 mg. (1 grain).

Narcotine is an alkaloid extracted from opium in 1861 by Foster. Like papaverine it is an isoquinoline compound, its formula being given below. Upon treatment with oxidizing agents it breaks up into *cotarnine* and opianic acid.

Narcotine



Papaverine



Narcotine is not narcotic but is useful in treating headache, cough and mild pain.

Group VI.—Alkaloids Whose Structure is Little Understood

Physostigmine.—After considerable controversy, participated in by Salway, Barger, Brady, and Polonovski, the graphic formula submitted by the latter has received general acceptance. It is given below.

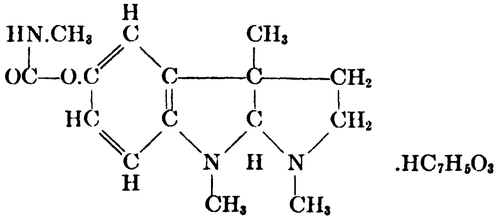
A characteristic reaction of physostigmine is the red-blue color play produced when its ammonium hydroxide solution is evaporated on a water bath and acidified with acetic acid; as well as the color produced with nitric acid.

The alkaloid is obtained from calabar bean by extracting same in fine powder with warm alcohol containing 0.1 per cent tartaric acid. The alcohol is distilled from the tincture, the residue treated with water, the filtrate shaken with ether to remove color, and then made alkaline with potassium bicarbonate, and again shaken out with ether, which this time extracts the free alkaloid, which is obtained by evaporation of the ethereal solution.

Physostigmine, or *eserine*, as it is sometimes called, is recognized by the Pharmacopœia in the form of salicylate, which is described in detail on the succeeding page.

PHYSOSTIGMINÆ SALICYLAS—Physostigmine Salicylate

(Physostig. Salicyl.—Eserine Salicylate)



$C_{15}H_{21}O_2N_3.HC_7H_5O_3$ Molecular weight, 413.23

The salicylate of an alkaloid obtained from the dried ripe seed of *Physostigma venenosum* Balfour (Fam. *Leguminosæ*).

Storage.—Preserve in air-tight containers and protected from light.

Summarized Description.

Colorless or faint yellow, shining, acicular or short columnar crystals; turns red on exposure to light and air; very poisonous; soluble in about 75 parts of water and in about 13 parts of alcohol and in about 9 parts of chloroform; less soluble in ether. For details, see U.S.P., p. 289.

For *tests for identity* and for *impurities* (sulfate, carbonizable substances), see U.S.P., p. 289.

Remarks.—Salts of physostigmine are very deliquescent, and the pharmacist is warned against buying even so small a quantity as 1 Gm. unless the whole quantity is to be dispensed at one time; nor is it advisable to keep the physostigmine salts in solution, as the originally colorless solution turns a dark red. The larger manufacturers of alkaloids now dispense physostigmine in 1-grain tubes, which are sealed by a blowpipe, thus precluding all contact with the atmosphere. Such is the only way that the pharmacist should keep eserine in stock.

Physostigmine salts are used almost entirely as miotics—that is, for producing contraction of the pupil of the eye. If given internally, they are used as tonics.

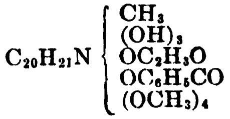
Dose.—2 mg. (1/30 grain).

Aconitina (U.S.P. X), or *Aconitine*, $C_{34}H_{47}O_{11}N$, is an alkaloid obtained from aconite. It occurs in colorless or white crystals. It is extremely poisonous and when highly diluted with water gives a tingling and numbing sensation to the tongue.

Extraction.—Powdered aconite is exhausted with amyl alcohol and the percolate shaken out with 0.2 per cent sulfuric acid. The acid solution is freed from resin and other impurities by shaking with ether, and is then made alkaline with sodium carbonate and shaken out with ether.

The crude alkaloid obtained by evaporation of the ethereal solution is purified by recrystallization from ether or from alcohol.

Composition.—Investigations of aconitine have developed its formula to the extent shown below:



$$C_{20}H_{21}N\left\{\begin{array}{l}CH_3\\(OH)_3\\OC_2H_3O\\OC_6H_5CO\\(OCH_3)_4\end{array}\right.$$

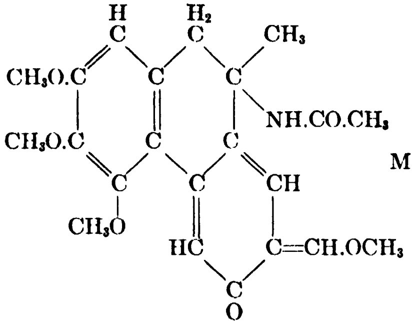
Remarks.—In former Pharmacopœias this chemical was interesting as being the most potent official substance; being administered in the smallest dose. In fact, its use internally is not advisable.

Medical Properties.—Like aconite.

Dose.—0.15 mg. (1/400 grain).

COLCHICINA—Colchicine

$C_{22}H_{25}O_6N$



Molecular weight, 399.20

An alkaloid obtained from *Colchicum autumnale* Linné (Fam. *Liliaceæ*).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Pale yellow amorphous scales or pale yellow amorphous powder; darkens on exposure to light; extremely poisonous; soluble in about 22 parts of water; very soluble in alcohol and in chloroform; less soluble in ether and benzene; insoluble in petroleum benzin; aqueous solution is levorotatory and of a yellow color; melts between 142° and 146° C. For details, see U.S.P., p. 128.

For *tests for identity* and for *impurities* (colchiceine, chloroform), see U.S.P., p. 128.

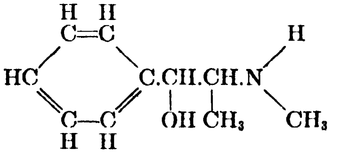
Extraction.—Use the Chemnitius method described under Pilocarpine (p. 904) except that the final residue of the crude alkaloid may be purified by crystallization from alcohol.

Medical Properties.—Like colchicum (p. 935).
Dose.—½ mg. (1/120 grain).

Arecolinæ Hydrobromidum (N.F. VI), $C_8H_{13}O_2N.HBr$, is the alkaloid derived from areca. It is used in tapeworm in dogs. It is administered subcutaneously to dogs in doses of 1/80 grain per pound of body weight and to horses in doses of 1/2 grain per pound of body weight.

EPHEDRINA—Ephedrine
(Ephedrin.)

$C_{10}H_{15}ON$



Molecular weight, 165.13

An alkaloid obtained from *Ephedra equisetina* Bunge, *Ephedra sinica* Stapf and other species of *Ephedra* (Fam. *Gnetaceæ*).

Storage.—Preserve in well-closed containers, in a cool place and protected from light.

Summarized Description.

Unctuous, almost colorless solid or white colorless crystals; soluble in water, alcohol, chloroform, ether and liquid petrolatum; melts between 34° and 40° C. For details, see U.S.P., p. 144.

For *tests for identity* and for *impurities* (chloride, sulfate), see U.S.P., p. 144.

Remarks.—This alkaloid of *ephedra* (p. 939) belongs chemically more nearly to the class of nitrogenous substances which include epinephrine (p. 817). In most alkaloids, the nitrogen atom is located in the pyridine or quinoline ring. From the formula given above it will be noted that the nitrogenation of ephedrine is found in the side chain as it is in epinephrine.

Medical Properties.—While used internally as a vasoconstrictor like epinephrine, its chief use is as a spray in the treatment of asthma, hay fever, and nasal catarrh. No oral dose is assigned the free alkaloid by the Pharmacopœia.

EPHEDRINÆ HYDROCHLORIDUM—Ephedrine Hydrochloride

(Ephedrin. Hydrochlor.)

$C_{10}H_{15}ON.HCl$. Molecular weight, 201.60

Ephedrine Hydrochloride, when dried over sulfuric acid for twenty-four hours, contains not less than 80 per cent and not more than 82.5 per cent of anhydrous ephedrine ($C_{10}H_{15}ON$).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Fine, white, odorless crystals or powder; soluble in 3 parts of water and about 11 parts of alcohol; insoluble in ether; optical rotation, −33 degrees to −35.5 degrees. For details, see U.S.P., p. 145.

For *tests for identity*, for *impurity* (sulfate) and for *assay*, see U.S.P., p. 145.

Remarks.—This salt of ephedrine, like the sulfate, is more soluble in water than is the free alkaloid. It is therefore better adapted for use as intramuscular or intravenous injections.

Dose.—25 mg. (3/8 grain).

EPHEDRINÆ SULFAS—Ephedrine Sulfate

(Ephedrin. Sulf.)

$(C_{10}H_{15}ON)_2.H_2SO_4$. Molecular weight, 428.33

Ephedrine Sulfate, when dried over sulfuric acid for twenty-four hours, contains not less than 75.5 per cent and not more than 77.3 per cent of anhydrous ephedrine ($C_{10}H_{15}ON$).

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Fine white, odorless crystals or powder; freely soluble in water and in hot alcohol; difficultly soluble in cold alcohol; melts between 240° and 247° C.; optical rotation, −29.5 degrees to −32 degrees. For details, see U.S.P., p. 146.

For *tests for identity* and for *impurity* (sulfate) and for *assay*, see U.S.P., p. 146.

Remarks.—See Ephedrine Hydrochloride.

Dose.—25 mg. (3/8 grain).

ALKALOIDAL DRUGS

IPECACUANHA—Ipecac

(Ipecac.—Ipecacuanhæ radix P.I.)

Ipecac consists of the dried rhizome and roots of *Cephaëlis Ipecacuanha* (Brotero) A. Richard, known in commerce as Rio or Brazilian Ipecac, or of *Cephaëlis acuminata* Karsten, known in commerce as Cartagena, Nicaragua, or Panama Ipecac (Fam. *Rubiaceæ*).

Ipecac yields not less than 2 per cent of the ether-soluble alkaloids of ipecac and contains not more than 5 per cent of its overground stems, and not more than 2 per cent of other foreign organic matter.

Assay.—See U.S.P., p. 197.

Constituents.—*Emetine, cephaëline, psychotrine, emetoidine, ipecacuanhic acid* (a gluco-tannoid), a phytosterol, starch, etc.

Medical Properties.—Expectorant or emetic, according to dose.

Official Preparations.—*Fluidextract* (p. 269) and *Dover's powder* (p. 316). The fluidextract is a constituent of the *syrup* (p. 219).

Dose.—Of drug: Expectorant, 60 mg. (1 grain); emetic, 1 Gm. (15 grains).

Gelsemium (N.F. VI), or *yellow jassamine*, represents the rhizome and roots of *Gelsemium sempervirens*. It contains alkaloids (*gelsemine, gelsemicine, gelsemidine* and *gelsemoidine, sempervirine*, etc.), *scopoletin* (hydroxymethyoxy-coumarin, formerly called *gelseminic acid*), volatile oil, resin (consisting of a phytosterol; pentatriacontane, $C_{35}H_{72}$; and ipuranol, $C_{23}H_{38}O_2(OH)_2$; combined oleic, palmitic, stearic and linolic acids), etc. It is used as an antipyretic in 30-mg. doses. The Formulary recognizes the *extract* (p. 303), *fluidextract* (p. 271) and the *tincture* (p. 253).

Pareira (U.S.P. VIII; N.F. V) is the dried roots of *Chondodendron tomentosum* Ruiz et Pavon (Fam. *Menispermaceæ*).

The drug contains alkaloids (bebeerine, isobebeerine, chondodendrin, etc.), fat, starch, and tannin. It is used as a simple bitter and diuretic, in 30-grain doses.

ACONITUM—Aconite

(Aconit.—Aconite Root, Monkshood, Aconiti tuber P.I.)

Aconite is the dried tuberous root of *Aconitum Napellus* Linné and its subspecies and varieties containing aconitine (Fam. *Ranunculaceæ*).

Aconite, in the form of the tincture, administered subcutaneously to guinea-pigs, has a minimum lethal dose not exceeding 0.0004 cc. of tincture for each gram of body weight of guinea-pig. A new standard becomes effective July 1, 1937. Aconite contains not more than 5 per cent of its stems and not more than 2 per cent of other foreign organic matter.

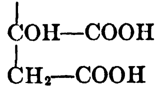
Assay.—See U.S.P., p. 32.

Constituents.—*Aconitine, napelline, neopelline, aconite acid,* etc. *Aconitine* consists of true aconitine, pseudoaconitine, aconine, pseudaconine, picraconitine, etc.

Remarks.—Aconite is a tuberous root from the *Ranunculaceæ*, or crowfoot family. Its well-known poisonous property is due to its alkaloid, aconitine, which is supposed to exist in the root as the salt of aconitic acid. This acid is closely allied to citric acid, as a side-by-side comparison formula will show:

Citric acid

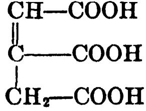
$H_3C_6H_5O_7$



$$\begin{array}{l} \mathrm{CH_2COOH} \\ | \\ \mathrm{COH{-}COOH} \\ | \\ \mathrm{CH_2{-}COOH} \end{array}$$

Aconitic acid

$H_3C_6H_3O_6$



$$\begin{array}{l} \mathrm{CH{-}COOH} \\ \| \\ \mathrm{C{-\!-}COOH} \\ | \\ \mathrm{CH_2{-}COOH} \end{array}$$

Like citric acid, aconitic acid is not poisonous. It is found in several plants other than aconite; for instance, sorghum and yarrow.

Medical Properties.—Of value in fevers produced from colds, neuralgia, etc. Locally as a local irritant and anesthetic. The *tincture* (p. 243) is official.

Dose.—60 mg. (1 grain).

Berberis (U.S.P. VIII; N.F. VI), or *Oregon grape root,* is "the rhizome and roots of species of the section *Mahonia* De Candolle of the genus *Berberis* Linné." It contains *berberine,* $C_{20}H_{17}NO_4$ (p. 924), *oxycanthine,* $C_{19}H_{21}NO_3$, *berbamine,* $C_{18}H_{19}NO_3$, etc. It is used as a tonic and stimulant in 30-grain doses.

Colchici Cormus (U.S.P. X; N.F. VI) is the dried corm of *Colchicum autumnale.* It contains *colchicine, colchiceine,* fat, gum, starch, inulin, etc. Two portions of the colchicum plant are medicinal: the "corm" and the seed of *Colchicum autumnale,* a pretty little liliaceous plant called "meadow-saffron," that decks the pastures of South

Germany with beautiful pink flowers during the month of September. A "corm" is a variety of tuber, the most familiar example of a tuber being the Irish potato. A thick, fleshy stem part, growing underground and designed as the storehouse for food for the next year's growth, is called a tuber, and colchicum root is a modification of a tuber called a corm. The *fluidextract* (p. 271) and the *strong tincture* (p. 255) are recognized by the Formulary.

Colchicum corm and seed are of great value in gout. Its use, however, must not be long continued, as it soon irritates the stomach and intestines. *Dose.*—Of drug, 250 mg. (4 grains).

COLCHICI SEMEN—Colchicum Seed

(**Colch. Sem.**—Colchici semen P.I.)

Colchicum Seed is the dried ripe seed of *Colchicum autumnale* Linné (Fam. *Liliaceæ*). Colchicum Seed yields not less than 0.45 per cent of colchicine.

Assay.—See U.S.P. p. 127.

Constituents.—*Colchicine, colchiceine,* fruit sugar, mucilage, tannin, fixed oil (6 to 8 per cent).

Medical Properties.—Like the corm. The *tincture* (U.S.P.) (p. 247), and *fluidextract* (N.F.) (p. 271) are official.

Dose.—200 mg. (3 grains).

Sanguinaria (N.F. VI), or *blood root,* represents the rhizome and roots of *Sanguinaria canadensis.* It contains *sanguinarine, chelerythrine, protopine, berberine,* resins, etc.

It is called blood root because, in the spring, the fresh rhizome, when broken, exudes a red juice. Likewise the dried drug is deep red in the interior.

It is used as a nauseant expectorant in 2-grain doses. The Formulary recognizes the *fluidextract* (p. 271), and the *tincture* (p. 254).

Spigelia (U.S.P. IX), or *pinkroot,* represents the rhizome and roots of *Spigelia marilandica.* It contains *spigeline* (volatile alkaloid), volatile oil, resins, etc. It is used as a vermifuge in 4-Gm. doses.

Hydrastis (U.S.P. X; N.F. VI), or *golden seal,* consists of the dried rhizome and roots of *Hydrastis canadensis.* It contains *hydrastine, berberine, canadine,* resin, starch, etc. This is an American drug, which has obtained world-wide reputation although, at present, under the ban of the medical members of the U.S.P. Revision Committee. Note its two leading constituents, of which the hydrastine should be white. Hydrastine is very expensive, hence the cheap yellow berberine is often substituted for it. Note that it is berberine which gives the drug the characteristic yellow color, which suggested the synonym, golden seal. Hydrastis is a bitter stomachic, useful in catarrhal trouble, hence of value for injection in gonorrhea. The *extract* (p. 303), the *fluidextract* (p. 271) and the *tincture* (p. 253) are recognized by the Formulary. *Dose.*—2 Gm. (30 grains).

VERATRUM VIRIDE—Veratrum Viride

(**Verat. Vir.**—Green Hellebore, American Hellebore)

Veratrum Viride consists of the dried rhizome and roots of *Veratrum viride* Aiton (Fam. *Liliaceæ*).

Veratrum Viride contains not more than 5 per cent of its stems or other foreign organic matter, and yields not more than 4 per cent of acid-insoluble ash.

Constituents.—*Jervine, pseudojervine, rubijervine, veratroidine, cevadine.* White veratrum contains veratrine and also the alkaloids above mentioned. The official veratrine comes from cevadilla seed (p. 923).

Remarks.—While U.S.P. VIII recognized both American hellebore and white hellebore (from *Veratrum album*) under the title "Veratrum"; in the present edition only *Veratrum viride* is official. It is used as a sedative, emetic and diuretic. The *tincture* (p. 252) is official.

Dose.—100 mg. (1½ grains).

CINCHONA—Cinchona
(Cinch.—Peruvian Bark)

Cinchona is the dried bark of the stem or of the root of *Cinchona succirubra* Pavon et Klotzsch or its hybrids, known in commerce as Red Cinchona, or of *Cinchona Ledgeriana* (Howard) Moens et Trimen, *Cinchona Calisaya* Weddell or hybrids of these with other species of *Cinchona*, known in commerce as Calisaya Bark or as Yellow Cinchona (Fam. *Rubiaceæ*).

Cinchona yields not less than 5 per cent of the alkaloids of Cinchona.

Assay.—See U.S.P., p. 121.

Constituents.—*Quinine, quinidine, cinchonine, cinchonidine* and many other alkaloids: quinic, quinovic and cinchotannic acids; etc.

Incompatibilities (of tincture).—See prescription No. 37 of Chapter LIX.

Remarks.—Cinchona ranks among the most important of the official drugs. U.S.P. XI gives a wide range of selection of the cinchona barks grouping under the head, *Cinchona,* bark containing 5 per cent of the alkaloids peculiar to the species.

Time forbids an extended sketch of the origin and history of the cinchona barks, but the student is advised to read the subject in the dispensatories. Here need only be said that the general introduction of the bark was due to the Countess of Chinchon, wife of a viceroy of Peru, who was cured of malaria by the use of the drug in the sixteenth century, and since then it has gained the esteem of the entire world. The reckless collection of the drug by chopping down wild trees, with no attempt to plant new ones in their stead, threatened the extermination of this valuable drug, but, fortunately, this danger was averted by the commencement of the systematic cultivation of the drug by the Dutch in Java and by the English in India, who have taken most of the business from its first home—Chile and Peru.

Note that of the large number of alkaloids separated from cinchona, but four—quinine, quinidine, cinchonine, cinchonidine—are worthy of careful study.

Note also that cinchona contains a large amount of tannin. This explains the well-known prescription incompatibility, the inky liquid obtained by mixing preparations of cinchona with iron salts (p. 1060); hence in preparing such pharmaceuticals as elixir of cinchona and iron the cinchona percolate must be "detannated" before adding the iron salt.

Mention must be made of a former official product of cinchona, which was dropped in the revision of 1890; a substance called *chinoidine.* In the days when quinine was worth $4 to $5 an ounce, a cheaper cinchona product was demanded. This was found in chinoidine, whose efficiency was due to the imperfect methods then employed in making quinine. Quinine is separated from the other cinchona alkaloids by crystallization, and in the old process, after the mother liquor had been concentrated several times, thus yielding most of the four official alkaloids, it was evaporated to a brown mass, still containing some of the four alkaloids, as well as all the minor bodies found in the bark. But the old-time primitive methods of extraction have given place to modern processes, by which almost all of the important alkaloids are won from the cinchona, leaving the mother liquor practically inert. Hence chinoidine of today is almost valueless and in the pharmacopœial revision of 1890 it was omitted.

Medical Properties.—Febrifuge (quinine is a specific in malarial fever), tonic, astringent. Official preparation: *compound tincture* (p. 246).

Dose.—1 Gm. (15 grains).

Granatum, or *pomegranate,* is the bark of the stem and root of *Punica Granatum.* It contains Pelletierine (U.S.P.), punicotannic acid, etc. Note that the official drug is the bark of the stem and root, not the rind of the fruit, which is so popular in the southern

States, as a dysentery remedy. It is used as a tenifuge and is administered preferably as the alkaloid pelletierine, or as *fluidextract*. *Dose.*—Of drug, 2 Gm. (30 grains).

Areca (N.F. VI), or *betel nut*, is the dried ripe seed of *Areca Catechu.* It contains *arecoline*, *arecaine* and a third alkaloid. It also contains tannin and a fixed oil. It has been used in India for centuries as a masticatory. It has been stated that one-tenth of the world's people in the Orient are betel chewers. Medicinally it is used for the expulsion of tapeworm. In this country it is used only in veterinary practice. *Dose.*→For dogs 2–4 Gm. (30–60 grains); for sheep 4–8 Gm. (1–2 drachms).

Aspidosperma (U.S.P. IX), or *quebracho*, is the bark of *Aspidosperma Quebracho blanco.* It contains alkaloids (*aspidospermine*, *aspidospermatine*, *quebrachine*, etc.), quebrachol, $C_{20}H_{34}O$; quebrachit, $C_6H_{11}(OCH_3)O_5$; tannin, etc.

Quebrachine, $C_{22}H_{28}O_3N_2$, is said to be identical with *yohimbine*, the alkaloid of yohimbe bark (from *Corynanthe Yohimbe*), but the question is not definitely settled. Yohimbine is considerably used in Europe as an aphrodisiac.

Quebracho is used as a tonic and also as a dysentery remedy.

Dose.—4 Gm. (60 grains).

Pilocarpus (U.S.P. IX), or *jaborandi*, represents the leaflets of *Pilocarpus Jaborandi* and of *Pilocarpus microphyllus.* The two varieties are known as Pernambuco and Maranham jaborandi respectively from the two Brazilian towns from which they enter the market. Jaborandi contains alkaloids (*pilocarpine*, *isopilocarpine*, *pilocarpidine*, *carpilline*, etc.); volatile oil; resin; etc. It is used as a diaphoretic and sialogogue in 2-Gm. doses. While jaborandi and its preparations were dropped in the recent pharmacopœial revision, its alkaloidal salts, *pilocarpine hydrochloride* and *nitrate* (p. 905) are official.

Coca (U.S.P. VIII) is the dried leaflets of *Erythroxylon Coca* and *Erythroxylon Truxillense.* The drug contains *cocaine*, *hygrine*, cocatannic acid, etc. It has been used by the natives of Peru, since the earliest times as a stimulant. The Indians chew the leaves mixed with ashes, and are then capable of performing such hard tasks as climbing mountains with loaded backs, practically abstaining from food during the trip. Its use as a tonic in Europe and North America covers a period of many years, but its great consumption began in the early eighties, with the discovery of the remarkable local anesthetic action of its alkaloid, cocaine, made official in 1890 in the form of *cocaine hydrochloride.* The frightful abuse of cocaine has extended to coca leaves as well; hence the revision committee decided to delete from the Pharmacopœia, coca and all of its preparations.

Coca, as suggested above, is used as a stimulant, in 30-grain doses.

BELLADONNÆ FOLIUM—Belladonna Leaf

(**Bellad. Fol.**—Belladonnæ Folia U.S.P. X, Belladonna Leaves, Deadly Nightshade Leaf, Belladonnæ folium P.I.)

Belladonna Leaf consists of the dried leaves and tops of *Atropa Belladonna* Linné (Fam. *Solanaceæ*).

Belladonna Leaf yields not less than 0.3 per cent of the alkaloids of Belladonna Leaf, and contains not more than 3 per cent of belladonna stems over 10 mm. in diameter. It yields not more than 3 per cent of acid-insoluble ash.

Assay.—See U.S.P., p. 84.

Constituents.—*Atropine*, *hyoscyamine*, *belladonnine*, and other alkaloids, chlorophyll, etc. Kilmer and others incline to the belief that hyoscyamine is the real narcotic principle of the solanaceous drugs.

Remarks.—Belladonna is derived from the "deadly nightshade," *Atropa Belladonna*, the leaves and root of which are official. Both contain atropine, which dilates the pupil of the eye, making it large and lustrous. From this property the drug gets its name, which is Italian for "pretty lady." Besides atropine, the drug contains two other official alkaloids, hyoscyamine and hyoscine, these two being, of course, named after hyoscyamus, in which they are first found. All three of these alkaloids are found in various proportions in many of the plants of the Solanaceæ—the nightshade family—to which both belladonna and hyoscyamus belong, and all three, by reason of the property of dilating the pupil, are called the *mydriatic alkaloids.* Hyoscyamine and atropine are isomeres—both have the same chemical formula. In fact, so similar are they that they can be distinguished only by the differing behavior of their gold salts.

Medical Properties.—Stimulates the higher centers, hence used in asthma and to quicken the pulse; used to modify the action of vegetable purgatives, as is shown in *compound laxative pills,* and several other pills of the National Formulary in which extract of belladonna leaves is employed. Used externally in neuralgia. Official preparations: the *extract* (p. 299), and the *tincture* (p. 244). From the extract, the *ointment* (p. 366) is made.

Dose.—60 mg. (1 grain).

BELLADONNÆ RADIX—Belladonna Root

(Bellad. Rad.—Deadly Nightshade Root)

Belladonna Root is the dried root of *Atropa Belladonna* Linné (Fam. *Solanaceæ*).

Belladonna Root yields not less than 0.45 per cent of the alkaloids of Belladonna Root, and contains not more than 10 per cent of its stem bases and woody crowns and not more than 2 per cent of other foreign organic matter. It yields not more than 4 per cent of acid-insoluble ash.

Assay.—See U.S.P., p. 85.

Constituents.—Like the leaves, except for absence of chlorophyll.

Remarks.—Note that the root contains more mydriatic alkaloids than do the leaves (root, $\frac{45}{100}$ of 1 per cent; leaves, $\frac{3}{10}$ of 1 per cent), hence it is administered in smaller dose.

Medical Properties.—Like the leaves. The *fluidextract* (p. 264) and the *plaster* (p. 377) are official.

Dose.—Of drug, 45 mg. ($\frac{3}{4}$ grain).

STRAMONIUM—Stramonium

(Stramon.—Jimson Weed, Jamestown Weed)

Stramonium consists of the dried leaves and flowering tops of *Datura Stramonium* Linné (Fam. *Solanaceæ*).

Stramonium yields not less than 0.30 per cent of the alkaloids of Stramonium, contains not more than 3 per cent of stems over 8 mm. in diameter, and yields not more than 4 per cent of acid-insoluble ash.

Assay.—See U.S.P., p. 361.

Constituents.—Atropine, hyoscine, hyoscyamine, small amount of odorous volatile oil, chlorophyll. The constituent *daturine* has been proved a mixture of atropine and hyoscyamine.

Remarks.—Stramonium is the leaves of *Datura Stramonium,* which is the well-known "jimson weed," a plant growing all over the United States, Europe, and Asia. It is said that the plant has become so widely distributed through those curious people, the gypsies, who travel all over the world, carrying with them stramonium seed—for criminal uses it is said. It is also claimed that it was the active constituent of the witches' brew of medieval times. Note that stramonium belongs to that plant family called the *Solanaceæ,* or nightshade family, which furnishes such valuable drugs as belladonna and hyoscyamus, and also includes several of our best known vegetables, like Irish potato, tomato, and eggplant.

Belladonna, hyoscyamus, and stramonium contain the three mydriatic alkaloids, atropine, hyoscine, and hyoscyamine. Quite often we find such chemical similarities existing between members of the same plant family—a very striking fact when we consider that the method by which we classify plants has nothing to do with chemistry.

Incompatibilities (*of tincture*).—See prescription No. 63 of Chapter LIX.

Medical Properties.—Like belladonna. The *extract* (p. 302) and the *tincture* (p. 251), are official.

Dose.—75 mg. (1¼ grains).

Stramonium seeds, which were recognized by the Pharmacopœia of 1890, never enjoyed the same popularity as the leaves, hence were dropped from the eighth edition. They contained the same alkaloids and were used similarly to the leaves and given in the same dose.

HYOSCYAMUS—Hyoscyamus

(Hyosc.—Henbane, Hyoscyami folium P.I.)

Hyoscyamus is the dried leaf, with or without the tops, of *Hyoscyamus niger* Linné (Fam. *Solanaceæ*).

Hyoscyamus yields not less than 0.040 per cent of the alkaloids of Hyoscyamus and contains not more than 25 per cent of its stems, none of which is more than 7 mm. in thickness. It yields not more than 12 per cent of acid-insoluble ash.

Assay.—See U.S.P., p. 193.

Constituents.—Hyoscyamine and hyoscine.

Remarks.—Hyoscyamus is commonly called henbane. Note that the drug is much weaker in mydriatic alkaloids than are belladonna and stramonium leaves, the last two being required to contain respectively 3⁄10 of 1 per cent of alkaloids, while the requirement for hyoscyamus is but 4⁄100 of 1 per cent.

Medical Properties.—Similar to belladonna, but preferable to the latter drug in insomnia and for relieving the excitement of insanity. Official preparations: *extract* (p. 301) and *tincture* (p. 248). The fresh leaves steeped in a fixed oil along with other drugs and aromatics is highly popular in Europe under the name *Baume Tranquille,* as a remedy for earache, and for general use as a liniment. See *compound oil of hyoscyamus* (N.F. V).

Dose.—Of drug, 200 mg. (3 grains).

Scopola (U.S.P. VIII) is the dried rhizome of *Scopola Carniolica.* It contains *scopolamine* (identical with hyoscine); some *hyoscyamine, scopoletin* (hydrox-methoxy-coumarin), fat, sugar, etc. It was accorded pharmacopœial recognition as a source of scopolamine and because its extract is used by some plaster-makers for their so-called "belladonna plasters." If used, it is, like belladonna and hyoscyamus, a sedative and narcotic. *Dose,* ¾ grain.

Tobacco, the leaves of *Nicotiana tabacum,* was official in former Pharmacopœias. It was formerly highly esteemed as a vulnerary, but is little used as a drug by intelligent physicians. A decoction of tobacco in which corrosive sublimate has been dissolved makes a satisfactory *bedbug poison.*

Lobelia (U.S.P. X; N.F. VI) or *Indian tobacco* consists of the dried leaves and tops of *Lobelia inflata.* It contains *lobeline,* $C_{22}H_{27}O_2N$, a liquid alkaloid; *lobelidine, lobelic acid,* resin, etc. This is a remedy highly esteemed by the natives and early colonists of North America. It was brought into medical prominence largely through the efforts of eclectic practitioners. It is used as an expectorant and emetic. It is poisonous in large doses. The *fluidextract* (p. 271) and the *tincture* (p. 253) are recognized by the Formulary. *Dose,* 100 mg. (1½ grains).

Ephedra, or *Ma Huang,* is the herb *Ephedra sinica,* which has been used by Chinese physicians for over 5000 years. From it in 1887 Nagai isolated the principle *ephedrine* (p. 932) while Chen since 1923 has given the drug and its active principle such extensive study that Ephedra is now one of our most popular medicaments. Ephedra was used in China as a diaphoretic and febrifuge, while ephedrine is now used in this country as a broncho-dilator in asthma and in the treatment of nasal catarrh.

Scoparius (**U.S.P. VIII; N.F. V**), **or *broomtop*, is the dried tops of *Cytisus Sco-***

parius (Linné) Link (Fam. *Leguminosæ*). The drug contains *sparteine* (liquid alkaloid), *genisteine* and *sarothamnine* (also alkaloids), *scoparin* (neutral principle), volatile oil, tannin, etc. Broom is the "planta genista," from which the famous Plantagenet family took its name. It is not the broomstraw from which the modern American brooms used in sweeping are made, albeit a certain druggist was once known to fill a prescription for "decoction of broom" from the straw of that homely domestic article. Scoparius is used as a diuretic. *Dose*, 15 grains.

Chelidonium.—The entire plant, *Chelidonium majus*, was official in the Pharmacopœia of 1890. It, like the plant yielding opium, belongs to the natural order Papaveraceæ, the poppy family, and its juice also is somewhat narcotic. It contains the alkaloids, *chelidonine* and alpha and beta *homochelidonine*, *berberine* and also *chelidonic acid*. The drug is not used very largely. To the poppy family belongs also sanguinaria.

Conium (U.S.P. VIII; N.F. V) is the full-grown but unripe fruit of *Conium maculatum*. It contains coniine, conhydrine, a trace of volatile oil, and fixed oil. It, like anise, coriander, fennel, and caraway, is a fruit of the natural order *Umbelliferæ*, and closely resembles anise in appearance—so much so that it has been confused with that drug, and with serious results. Unlike the four fruits just mentioned, it contains little or no aromatic oil, and does contain the poisonous liquid alkaloid coniine. This alkaloid has the peculiar odor of mice's urine, thus affording a good method of distinguishing conium from anise. Conium is that "seed," or, more correctly, that fruit, which, when triturated with solution of soda, gives off the odor of mice's urine. Conium is narcotic and sedative and is given in 3-grain doses.

NUX VOMICA—Nux Vomica

(Nux Vom.—Strychni semen P.I.)

Nux Vomica is the dried ripe seed of *Strychnos Nux-vomica* Linné (Fam. *Loganiaceæ*). Nux Vomica yields not less than 1.5 per cent of strychnine.
Assay.—See U.S.P., p. 244.

Constituents.—*Strychnine, brucine*, and other alkaloids; *igasuric acid; loganine;* fat; and albumin. Hobart believes that copper is not a normal constituent of nux vomica.

Remarks.—The "buttons" of nux vomica are very characteristic, and their silky appearance is due to the fine hairs with which they are covered. The fixed oil sometimes proves troublesome pharmaceutically, the alcoholic preparations frequently turning milky on addition of water.

Medical Properties.—Nervous stimulant and bitter tonic. Very poisonous. Antidote is chloral hydrate, which, however, merely lessens the force of the tetanic convulsions, and should be used only under direct supervision of the physician. In some respects a better antidote is an alkaloidal precipitant, such as tannin, compound solution of iodine, or potassium permanganate. The *extract* (p. 302) and *tincture* (p. 250) of nux vomica are official.

Dose.—100 mg. (1½ grains).

Physostigma (U.S.P. IX) or *Calabar bean*, represents the seed of *Physostigma venenosum*. It contains alkaloids (*physostigmine* or *eserine*, $C_{15}H_{21}O_2N_3$; geneserine, $C_{15}H_{21}O_3N_3$; *physovenine*, $C_{14}H_{18}O_3N_2$); *calabarol*, $C_{23}H_{54}O_2(OH)_2$; phytosterols and other alcohols (trifolianol, stigmasterol, silosterol, glycerides of behenic, stearic, oleic, palmitic, linolenic acids, etc.

It is called "Calabar bean," from that section of Africa where it grows. Its alkaloid, physostigmine, is official as the salicylate, which is less deliquescent than the other salts (p. 931). Similarly to strychnine, physostigmine (p. 931) is used for contracting the pupil of the eye—is a miotic, just the reverse of the mydriatic (p. 909). For this reason miotic drugs (like strychnine and physostigmine) have been suggested as antidotes to mydriatics (such as belladonna and hyoscyamus), and similarly mydriatics have been used as antidotes to miotics. Such reasoning is not, however, necessarily logical. *Dose.*—100 mg. (1½ grains).

Staphisagria (U.S.P. IX), or *stavesacre*, represents the seed of *Delphinium Staphisagria*. It contains alkaloids (*delphinine, delphinoidine*); *staphisagrin*, etc.

Delphinium Staphisagria is a plant closely related to the garden larkspur, *Delphinium consolida*. The former plant has odd-shaped flowers resembling the larkspur.

Stavesacre is a very potent remedy, and is used chiefly as a wash for body-lice. When used internally it acts something like aconite. It is rarely employed, however, except externally. *Dose.*—60 mg. (1 grain).

Sabadilla or *cevadilla seeds*, the seeds of *Asagræa officinalis*, has already (p. 923) been mentioned as the commercial source of veratrine. That substance, it will be recalled is a mixture of several alkaloids, including true veratrine, cevadine and cevadilline.

ERGOTA—Ergot

(Ergot.—Ergot of Rye, Secale cornutum P.I.)

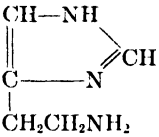
Ergot is the dried sclerotium of *Claviceps purpurea* (Fries) Tulasne (Fam. *Hypocreaceæ*), developed on rye plants.

Ergot, when assayed by the method herein directed, possesses a potency, per gram, equivalent to not less than 0.5 mg. of ergotoxine ethanesulfonate. It contains not more than 8 per cent of moisture and not more than 4 per cent of seeds, fruits and other foreign organic matter.

Storage.—Preserve under all conditions of storage and transportation in water-proof and air-tight containers.

Assay (biologic).—See U.S.P., p. 148.

Constituents.—The four alkaloids, *ergotoxin*, $C_{35}H_{41}O_6N_5$, or *hydroergotinine* (claimed to be the most active constituent of ergot); *ergotinine*, $C_{35}H_{39}O_5N_5$; *ergotamine* and *ergotaminine*, isomeres, $C_{33}H_{35}O_5N_5$; the simpler amino bodies, *tyramine* and *histamine*



sterols, including ergosterol (p. 747); *ergothioneine*, etc.

Dudley and Moir (1935) have isolated, in crystalline form, a new alkaloid which they call *ergometrine* and which they claim exhibits greater activity than any of the other ergot constituents. Thompson has isolated what is apparently the same alkaloid described by Dudley and Moir and has patented it under the name *ergostetrine*. This adds more confusion to an already confused situation. The "last word" (1936) is the statement issued by the Council on Pharmacy and Chemistry of the American Medical Association to the effect that Kharasch's *ergotocine*, Dudley and Moir's *ergometrine*, Stoll's *ergobasine* and Thompson's *ergostetrine* are probably identical. In view of this confusion, the American Medical Association suggests the use of a new generic name, *ergonovine*.

Remarks.—Ergot, according to the official definition, is "the dried sclerotium of *Claviceps purpurea* . . . developed on rye plants." Within this definition is found one of the most interesting life cycles in botany. At this place it need merely be said that *Claviceps purpurea* is a parasite, the spores of which settle upon the tender ovary of the rye plant from which they suck nutriment and develop into a hard brownish-purple fusiform growth, which is called the sclerotium.

There has been during the past decade much controversy over the evaluation and the presentation of ergot and its preparations. Former Pharmacopœias directed that ergot should be kept no longer than one year. Thompson's investigations indicate that the same age limit should be set for the fluidextract.

Medical Properties.—Used as an ecbolic (producing contraction of the uterus in childbirth) and for hemorrhages. Official preparation: the *fluidextract* (p. 267).

Dose.—2 Gm. (30 grains).

OPIUM—Opium

(Gum Opium)

Opium is the air-dried, milky exudation obtained by incising the unripe capsules of *Papaver somniferum* Linné or its variety *album* De Candolle (Fam. *Papaveraceæ*).

Opium in its normal, air-dried condition yields not less than 9.5 per cent of anhydrous morphine.

OPIUM GRANULATUM—Granulated Opium

(Opium Gran.)

Opium dried at a temperature not exceeding 70° C., and reduced to a powder, all of which will pass through a number 16 standard mesh sieve and not more than 10 per cent through a number 60 standard mesh sieve.

Granulated Opium yields not less than 10 per cent and not more than 10.5 per cent of anhydrous morphine. Granulated Opium of a higher morphine percentage may be reduced to the official standard by admixture with granulated opium of a lower percentage, or with any of the diluents permitted for powdered extracts under *Extracta* (U.S.P. XI, p. 152).

Storage.—Preserve in well-closed containers.

OPIUM PULVERATUM—Powdered Opium

(Opium Pulv.—Opii pulvis P.I.)

Opium dried at a temperature not exceeding 70° C., and reduced to a very fine powder.

Powdered Opium yields not less than 10 per cent and not more than 10.5 per cent of anhydrous morphine. Powdered Opium of a higher morphine percentage may be reduced to the official standard by admixture with powdered opium of a lower percentage, or with any of the diluents permitted for powdered extracts under *Extracta*.

Storage.—Preserve in well-closed containers.

Constituents.—*Morphine, codeine, narceine, narcotine,* and many other alkaloids, meconic acid, lactic acid, gum, etc. No starch.

Remarks.—Read carefully the pharmacopœial definition given above, and note that opium is "the air-dried milky exudation" obtained by cutting—"incising"—the unripe capsules of *Papaver somniferum.* The poppy capsules (or heads) found in drug stores are from the same plant, but are collected on ripening, when they do not contain so much milk juice. An analogous case is found in the fig, which abounds in milk juice when green and has scarcely any when ripe.

Papaver somniferum can grow as well in this country as it can in Asia Minor, and the only reason why opium is not produced here is that the incising of the capsule (slitting with a sharp knife without penetrating the capsule) is a laborious task performed by hand, and in such work America cannot compete with the cheap labor of the East. Note that the three official forms of opium given above, the moist gum (*gum opium* of commerce) containing not less than 9.5 per cent of morphine, the *powdered,* and the *granulated,* prepared by driving off the moisture from the gum and converting the dried mass either to powder or to granules, the latter made by moistening with alcohol and rubbing through a coarse sieve.

Both the powdered and the granulated must contain not less than 10 per cent nor more than 10.5 per cent of crystallized morphine.

Incompatibilities (*of tincture*).—See prescription No. 58 of Chapter LIX.

Medical Properties.—Sedative and narcotic. Poisonous. *Antidote,* stimulants (caffeine or coffee), electric shocks, flagellation. Above all, keep patient in motion. Official preparations. From the *moist gum* we make the *powdered* and the *granulated;* from the *powdered* we make the *camphorated tincture* (p. 251), and *powder of ipecac* and *opium* (p. 316); from the *granulated* we make the *tincture* (p. 250) which is really the *deodorized tincture* of former Pharmacopœias.

Dose.—Of all forms, 60 mg. (1 grain).

Opium Deodoratum (U.S.P. IX), or *denarcotized opium*, is prepared by extracting powdered opium with benzin, that solvent removing little from the drug but its heavy disagreeable narcotic odor. In the Pharmacopœia of 1890, ether was used as the deodorizing solvent, but it has been found that petroleum ether or even melted paraffin will do the work as thoroughly and more cheaply than does ether, and that without the loss of the narcotine (see p. 930).

BIBLIOGRAPHY

Pyridine.—(Source) Anderson, A., 80, 1851, 44 and 55. (Structure) Koener through Baeyer, A., 155, 1870, 282. (Manufacture) Koenigs, B., 12, 1879, 2341. (Uses) Kayser, A.Ph.A., 36, 1886, 486.

Quinoline.—(Structure) Koerner, through Baeyer, B., 12, 1879, 460. (Syntheses) Skraup, Ch. Cent., [3], 11, 1880, 359; Baeyer and Drewsen, B., 15, 1882, 2856. (Reactions) Skraup, B., 14, 1881, 1003; Miller, B., 23, 1890, 2252; Friedlander and Gohring, B., 16, 1883, 1835.

Phenyl-cinchonic Acid.—Doebner and Giesecke, A., 242, 1887, 291; Anon., Jl. A.M.A., 73, 1919, 427; Anon., C.A., 13, 1919, 2254; Davy, Jl. A.Ph.A., 8, 1919, 281; Nicolaier and Dohrn, C.A., 2, 1908, 2832; Heller, A.Ph.A., 59, 1911, 128; Barron, C.A., 18, 1924, 2762; Chemnitius, C.A., 22, 1928, 4718; Pasternack, Jl. Soc. Ch. Ind., 48, 1929, 150B.

Plasmochin.—Puckner, Jl. A.M.A., 89, 1927, 113; Kraus, *ibid.*, 90, 1928, 1064.

Acridine.—von Awers and Kraul, B., 58B, 1925, 543.

Acriflavine.—Benda, B., 45, 1912, 1787; Browning, Yearbook, A.Ph.A., 6, 1917, 454; Thieme, *ibid.*, 10, 1921, 443; Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 459.

Proflavine.—Hirschfelder, see above.

Rivanol.—Hirschfelder, see above; Anon., Jl. Soc. Ch. Ind., 48, 1929, 410.

Alkaloids.—(General) Huebner, Ch. Zt., 35, 1911, 146; 36, 1912, 1493 and 1505; Macht, Jl. A.M.A., 64, 1915, 1493; Slack, Ph. Jl., 96, 1916, 71; Trier, Ch. Zt., 43, 1919, 146, 158, 173 and 189; Polonovski, C.A., 20, 1926, 3486; Schorn, Ph. Jl., 116, 1926, 113; Couch, A.J.P., 103, 1931, 242; Awe, C.A., 26, 1932, 5603. (History) Tschirch, Sch. Ap. Zt., 58, 1920, 349; Stocking, Pharm. Era, 58, 1924, 75. (Solubility) Scholtz, Arch. d. Pharm., 250, 1912, 418. (Reactions) Mayer, A.Ph.A., 10, 1862, 238; Wagner, A.Ph.A., 14, 1866, 191; Wilbert, Am. Dr., 61, 1913, 234; Lloyd, Jl. A.Ph.A., 5, 1916, 381 and 490; Beal and North, *ibid.*, 13, 1924, 889 and 1001; Capelli, C.A., 19, 1925, 223; Cumming and Brown, Jl. Soc. Ch. Ind., 47, 1928, 84T; Russo and Lobos, C.A., 23, 1929, 3051; Munch and co-workers, Jl. A.Ph.A., 21, 1932, 463; Travell, *ibid.*, 23, 1934, 689. (Extraction) Boiraux and Leger, Ph. Jl., [3], 5, 1875, 642 and 661.

Piperidine.—(Manufacture) Rochleder and Wartheim, A., 70, 1849, 62; Cahours, A.J.P., 25, 1853, 118. (Synthesis and structure) Ladenburg, A., 247, 1888, 50.

Coniine.—Gieseke, through Brandes, A.J.P., 1, April, 1829, 76; Ladenburg, A., 247, 1888, 81.

Piperin.—(Synthesis) Rügheimer, A.Ph.A., 31, 1883, 294. (Extraction) Cazeneuve and Caillot, A.Ph.A., 26, 1878, 618.

Pilocarpine.—(Synthesis) Hardy and Calmets, Ch. and Dr., 31, 1887, 90. (Structure) Jowett, Jl. Ch. Soc., 87, 1905, 794; Pinner, B., 38, 1905, 1510; Spaeth and Kanz, B., 58B, 1925, 513. (Extraction) Hager, Handb., 2, 1913, 624; Chemnitius, Jl. prakt. Ch., 118, 1928, 20.

Pelletierine.—(Composition) Tanret, Jl. de ph. et ch., [5], 1880, 434; Willstätter and Veraguth, B., 38, 1905, 1984; Hess and Eichel, B., 50, 1917, 368, 1192 and 1386; B., 51, 1918, 741; Tanret, Jl. ph. Ch., 15, 1917, 158; J. Soc. Ch. Ind., 39, 1920, 638A. (Extraction) Tanret, A.Ph.A., 26, 1878, 280.

Nicotine.—(Source) Posselt and Reimann, A.J.P., 3, 1831, 175. (Structure) Pictet and Crepieux, B., 28, 1895, 1904; Pinner, B., 26, 1893, 292.

Sparteine.—(History) Rentler, Sch. Wsch. Ch. Ph., 51, 1913, 91. (Structure) Moureu and Valeur, Ann. Chim. Phys., [8], 27, 1912, 379 and 388; Winterfeld, Arch. Pharm., 266, 1928, 2751. (Extraction) Mills, Jl. Ch. Soc., 15, 1862, 1.

Tropine.—(Structure) Ladenburg, B., 28, 1895, 2277; Merling, A., 216, 1883, 329; Willstätter, A., 317, 1901, 204 and 326, 1903, 1.

Atropine.—(Structure) Kraut, A.J.P., 36, 1864, 231; Ladenburg, B., 13, 1880, 254 and A., 217, 1883, 72; Ladenburg and Hundt, B., 22, 1889, 2590. (Synthesis)

Gilling, Ph. Jl., 82, 1909, 355. (Extraction) Anon., A.J.P., 6, 1834, 314; Duilius, Ch. Zt., 54, 1930, 182. (Test) Vitali, Zt. analyt. Ch., 20, 1881, 563. (Pharmacology) Macht, Jl. A.Ph.A., 11, 1922, 882; Mitchell, C.A., 17, 1923, 2452.

Homatropine.—(Synthesis) Ladenburg, A., 217, 1883, 82. (Pharmacology), Macht, Jl. A.Ph.A., 11, 1922, 882.

Hyoscyamine.—(Extraction) Thorey, Zt. Chem., 14, 1871, 58. (Synthesis) Amenomiya, Arch. d. Pharm., 240, 1902, 498.

Hyoscine.—(Extraction) Ladenburg, A., 206, 1881, 281. (Composition) Hesse, A., 271, 1892, 100; Schmidt, Arch. d. Pharm., 230, 1892, 206; 243, 1905, 559 and 247, 1909, 79; Dohme, A.Ph.A., 55, 1907, 502; King, Ph. Jl., 102, 1919, 226.

Scopolamine.—(Structure) Schmidt, Arch. Pharm., 247, 1909, 79 and 253, 1915, 497; Fabre, J. ph. ch., 24, 1921, 336; Gadamer and Hammer, Arch. Pharm., 259, 1921, 110.

Ecgonine.—(Structure) Gadamer and Johns, Arch. Pharm., 259, 1921, 227; Macht, Jl. A.Ph.A., 11, 1922, 882.

Cocaine.—(History) Anon., Am. Dr., 15, 1886, 178. (Structure) Willstätter, B., 31, 1898, 2655 and A., 326, 1903, 42; Einhorn and Willstätter, B., 27, 1894, 2439 and A., 280, 1894, 96; Tainter, Quart. Jl. Ph., 3, 1931, 583. (Synthesis) Gilling, Ph. Jl., 82, 1909, 355; Willstätter, C.A., 18, 1924, 399; Merck and co-workers, Jl. Soc. Ch. Ind., 43, 1924, 577B; Ishihara, C.A., 25, 1931, 4359. (Extraction) Sperber, Sch. Wsch. Ch. Ph., 50, 1912, 173. (Uses) Anon., Am. Dr., 13, 1884, 230; Duilius, Ch. Zt., 54, 1930, 31. (Properties) Smith, Quart. Jl. Ph., 1, 1929, 387; Rothlin, Ph. Jl., 127, 1931, 190. (Sterilization) Lesure, Jl. de ph. et ch., 27, 1908, 474 and 526; Liot, Jl. Soc. Ch. Ind., 44, 1925, 417B; Hok, Quart. Jl. Ph., 3, 1931, 643. (Tests) E'we, Jl. A.Ph.A., 9, 1920, 1180; Breteau, C.A., 22, 1928, 3263. (Incompatibilities) Bougcr, C.A., 8, 1914, 2219; Guyot, Jl. ph. ch., 11, 1915, 24. (Pharmacology) Bulson, Jl. A.M.A., 77, 1921, 1730; Macht, Jl. A.Ph.A., 11, 1922, 882.

Eucaines.—Merling, A.Ph.A., 45, 1894, 727; Heintz, A., 187, 1877, 214 and 191, 1878, 124; Fischer, B., 17, 1884, 1794; Parsons, Jl. Am. Ch. Soc., 23, 1901, 886.

Procaine.—(Nomenclature) Stieglitz, Jl. A.Ph.A., 7, 1918, 742. (Structure) Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 456. (Pharmacology) Bulson, Jl. A.M.A., 77, 1921, 1730; Hooper, A.J.P., 96, 1924, 473; Gold, C.A., 18, 1924, 2205; Régnier, Jl. Soc. Ch. Ind., 43, 1924, 766B.

Other Cocaine Substitutes.—Wichura, Jl. Soc. Ch. Ind., 38, 1919, 598; Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 456; Copeland, C.A., 20, 1926, 240 and 1850; LaWall, Drug Topics, 46, 1930, 244; Merz, Arch. Pharm., 270, 1932, 125.

Cinchonine.—(Structure) Rabe, A., 373, 1910, 85 and B., 55B, 1922, 522; Leger, Jl. ph. ch., 23, 1921, 274; Zwikker, C.A., 16, 1922, 2149. (Solubility) Hatcher, A.J.P., 106, 1934, 243.

Quinine.—(History) Pelletiere and Caventou, Jl. de Ph., 7, 1821, 49; White, Am. Dr., 68, Dec., 1920, 20; Waser, Schw. Ap. Zt., 59, 1921, 329, 345 and 353; Lloyd, Science, 59, 1924, 241; England, A.J.P., 102, 1930, 702; LaWall, *ibid.*, 104, 1932, 24. (Structure) Koenigs, B., 29, 1896, 372; Murray, Merck's Rep., 14, 1905, 237, 266 and 301; Rabe, see above; Leger, see above; Zwikker, see above; Erben and co-workers, B., 58B, 1925, 2854; Emde, C.A., 26, 1932, 1629. (Extraction) Field, Am. Dr., 21, 1892, 152 and 22, 1892, 28; Landrin, Comp. rend., 108, 1889, 750. (Tests) Brandes and Leber, A., 32, 1839, 370; Herapath, A.J.P., 29, 1857, 245; Ramsden and Lipkin, Jl. ph. ch., 19, 1919, 47; Hart, Jl. Soc. Ch. Ind., 40, 1921, 72T; Hargreaves, Jl. A.Ph.A., 15, 1926, 100; Winograd, also Eisenbrand, C.A., 25, 1931, 2808. (Tannate) Thomas, A.J.P., 22, 1850, 360; Anon., A.Ph.A., 59, 1911, 495. (Incompatibilities) Stevens, A.Ph.A., 36, 1888, 93. (Pharmacology) Piccinini, C.A., 22, 1928, 2407; Chopra and co-workers, C.A., 23, 1929, 2211; Niccolini, C.A., 23, 1929, 1175.

Quinotoxin.—Scoville, Bull. Pharm., 30, 1916, 336; Sollmann, Jl. A.M.A., 76, 1921, 999; Ruddiman and Lanwermeyer, Jl. A.Ph.A., 13, 1924, 1009 and 15, 1926, 11 and 1009.

Quinidine.—(Structure) Rabe, see above; Leger, see above. (Extraction) Field, see above; Hesse, A., 146, 1868, 358 and 166, 1873, 236. (Pharmacology) Anon., Jl. A.M.A., 77, 1921, 1822.

Totaquina.—Hooper, Quart. Jl. Ph., 2, 1929, 186.

Cinchonidine.—(Structure) Rabe, see above; Leger, see above. (Extraction) Field, see above; Koenigs and Kusmann, B., 29, 1898, 2186. (Test) Kerner, A.J.P., 34, 1862, 420.

Optochin.—Hirschfelder, Jl. A.M.A., 66, 1916, 377 and Jl. Ind. Ch., 15, 1923, 458; Oliver, Yearbook A.Ph.A., 5, 1916, 377; Kolmer, *ibid.*, 9, 1920, 617; Anon., Pharm. Era, 54, 1921, 252; Heffter, C.A., 17, 1923, 2345.

Vuzin.—Schaeffer, Yearbook A.Ph.A., 7, 1918, 522; Bylsma, C.A., 15, 1921, 1575; Birkholz, C.A., 17, 1923, 3379; Heffter, see above.

Eucuprin.—Bylsma, see above; Heffter, see above.

Strychnine.—(History) Pelletiere and Caventou, Jl. de Ph., 5, 1819, 145. (Structure) Perkin and Robinson, Jl. Ch. Soc., 97, 1910, 305; Olivieri-Mandala, C.A., 18, 1924, 838 and 19, 1925, 75; Robinson and co-workers, C.A., 23, 1929, 843; 24, 1930, 3244; 25, 1931, 3004 and Jl. Soc. Ch. Ind., 49, 1930, 184; Cortese, C.A., 24, 1930, 164. (Extraction) Henry, Jl. de Ph., [2], 16, 1830, 752. (Taste-masking) Ward and Munch, Jl. A.Ph.A., 19, 1930, 954 and 1057. (Tests) Poe and O'Day, Jl. A.Ph.A., 19, 1930, 1292; Giovanni, C.A., 24, 1930, 683; Wagenaar, C.A., 24, 1930, 683. (Antidotes) Young, Ph. Jl., 123, 1929, 420; Scremin, C.A., 24, 1930, 5877; Gold and Travell, Jl. Pharmacol. Exp. Therap., 52, 1934, 30, 259 and 345; *ibid.*, 53, 1935, 169.

Brucine.—(Structure) Perkin and Robinson, see above. (Test) Caventou and Pelletiere, Jl. de Ph., 12, 1819, 542.

Veratrine.—(History) Meissner, Schweigger's Jl., 25, 1819, 379; Pelletiere and Caventou, Jl. de Ph., 8, 1820, 353. (Extraction) British Pharmacopœia, 1867, 365.

Hydrastine.—(Structure) Freund and Rosenberg, B., 23, 1890, 404 and 417; Freund A., 271, 1892, 311; Danckwortt, Arch. d. Pharm., 250, 1912, 597; Rosenmund, Ber. d. Pharm. Ges., 29, 1900, 200. (Extraction) Schmidt and Wilhelm, Arch. d. Pharm., 226, 1888, 331. (Synthesis) Fritsch, A., 286, 1895, 18; Robinson and co-workers, Jl. Soc. Ch. Ind., 50, 1931, 10; Kindler and Peschka, Arch. Pharm., 270, 1932, 353.

Berberine.—(Structure) Richter, Arch. d. Pharm., 252, 1914, 193; Robinson, C.A., 12, 1918, 141; Perkin, C.A., 12, 1918, 1872; Spaeth and Lang, C.A., 16, 1922, 1778; Schultz, Jl. A.Ph.A., 15, 1926, 33; Feist and Awe, Arch. Pharm., 269, 1931, 660.

Hydrastinine.—(Structure) Freund, A., 271, 1892, 311. (Synthesis) Fritsch, A., 286, 1895, 111; Rosenmund, J. Soc. Ch. Ind., 38, 1919, 386A.

Opium Alkaloids.—Anon., Chemistry of the Opium Alkaloids, Supp. 103, U. S. Public Health Service, 1932, pp. 1–375.

Morphine.—(History) Anon., Ch. and Dr., 65, 1904, 437 and 501; Anon., Pharm. Era, 46, 1913, 593; Serturner, Jl. de Ph., 3, 1817, 436; Hanzlik, Jl. A.Ph.A., 18, 1929, 375. (Structure) Knorr and Horlein, B., 40, 1907, 3347; Klee, Arch. d. Pharm., 252, 1914, 212; von Braun, B., 47, 1914, 2312; Speyer, B., 49, 1916, 1287 and C.A., 16, 1922, 4181; Robinson, C.A., 17, 1923, 2584; Schopf, A., 452, 1927, 211; Boehm, Arch. Pharm. 271, 1933, 6. (Synthesis) Anon., Jl. Soc. Ch. Ind., 48, 1929, 241. (Extraction) Mohr, A., 35, 1840, 119; Calvert, Am. Dr., 23, 1893, 22; Dott, J. Soc. Ch. Ind., 37, 1919, 431R. (Crystallography) Wherry and Yanvosky, C.A., 14, 1920, 179. (Preserving solutions of) Norgaard, C.A., 16, 1922, 4245.

Heroin.—Dreser, A.Ph.A., 47, 1899, 735.

Apomorphine.—(Structure) Knorr, B., 37, 1904, 1926; Klee, see above. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1153. (Pharmacology) Gorrell and Gray, C.A., 22, 1928, 4639.

Codeine.—(Synthesis) Grimaux, A.Ph.A., 30, 1882, 401. (Structure) Gadamer and Klee, Arch. Pharm., 252, 1914, 211; Freund, C.A., 13, 1919, 2512 and 15, 1921, 834; Robinson, C.A., 17, 1923, 2584; Dieterle and Dickens, Arch. Pharm., 264, 1926, 278. (Phosphate) Schmidt, A.Ph.A., 39, 1891, 616.

Apocodeine.—De Ritis, C.A., 14, 1920, 3107.

Dionin.—McLang, C.A., 23, 1929, 1132.

Papaverine.—Pictet and Kramers, Am. Dr., 58, 1911, 31; Macht, Jl. Pharmacol. Exp. Therap., 7, 1915, 339; 11, 1918, 263 and 419; A.J.P., 92, 1920, 676 and Jl. A.Ph.A., 11, 1922, 882; Hirschfelder, Jl. Ind. Eng. Ch., 15, 1923, 456; Kreitmair, C.A., 26, 1932, 3297.

Narcotine.—Foster, A.J.P., 8, 1863, 150 and A.Ph.A., 17, 1869, 262; Crawford and Dohme, A.Ph.A., 50, 1902, 472; Chopra and co-workers, C.A., 24, 1930, 5865; Cooper and Hatcher, Jl. Pharmacol. Exp. Therap., 51, 1934, 411.

Cotarnine.—Bakoffen, A.Ph.A., 47, 1899, 735; Salway, Jl. Ch. Soc., 97, 1910; Hanzlik, Jl. A.M.A., 70, 1918, 1883; 72, 1919, 577 and 73, 1919, 1628; Anon., Yearbook A.Ph.A., 7, 1918, 512; Kindler and Peschka, Arch. Pharm., 270, 1932, 355.

Physostigmine.—(Structure) Salway, Jl. Ch. Soc., 101, 1912, 980 and 103, 1913, 351; Brady, *ibid.*, 103, 1913, 1821; Polonovski, C.A., 17, 1923, 3033 and 18, 1924, 231. Stedman and Barger, Jl. Soc. Ch. Ind., 44, 1925, 188B; Spaeth and Brunner, *ibid.*, 44, 1925, 422B; Polonovski, C.A., 19, 1925, 2957. (Extraction) Vée and Leven, Jl. de ph. et ch., [4], 1, 1865, 70. (Tests) Petti, A.Ph.A., 22, 1874, 272; Ekkert, Dr. Circ., 69, 1925, 146. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1155. (Color change) Hallauer, A.Ph.A., 48, 1900, 818. (Pharmacology) Mitchell, C.A., 17, 1923, 2452.

Ephedrine.—(Production) Emde, Ph. Zt., 74, 1929, 1570 and Arch. Pharm., 268, 1930, 83. (Structure) Gordon, Jl. A.Ph.A., 17, 1928, 1195. (Syntheses) Spaeth, B., 58B, 1925, 197; Manske and Johnson, Jl. Am. Ch. Soc., 51, 1929, 580 and 1906; Skita, Jl. Soc. Ch. Ind., 48, 1929, 579; Nagai and Kanao, Yearbook, A.Ph.A., 17, 1928, 726; Chen, Jl. A.Ph.A., 20, 1931, 110 and 339. (Standardization) Peterson, Jl. Ind. Eng. Ch., 20, 1928, 389. (Deterioration) Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1153.

(Pharmacology) Chen and Schmidt, Jl. Pharmacol., 24, 1924, 339; Curtis, C.A., 22, 1928, 4656; Moller, C.A., 24, 1930, 3281. (Synthetic substitutes) Gordon, see above; Miller and Piness, Jl. A.M.A., 91, 1928, 1033; Hartung and Munch, Jl. Am. Ch. Soc., 53, 1931, 1875; Cherbuliez, C.A., 25, 1931, 2133.

Aconitine.—(Structure) Freund and Beck, B., 27, 1894, 433; Carr, Jl. Ch. Soc., 101, 1912, 2241; Brady, Jl. Ch. Soc., 103, 1913, 1821; Swanson, Jl. A.Ph.A., 13, 1925, 1108. (Extraction) Geiger, A.J.P., 6, 1834, 321; Williams, Ph. Jl., [3], 18, 1887, 238; Chemnitius, Jl. prakt. Ch., 118, 1928, 29.

Colchicine.—(Structure) Zeisel, J. B., 1888, 2, 2293; Windaus, Jl. Soc. Ch. Ind., 43, 1924, 805B; Castelain, Dr. Circ., 70, 1926, 926; Matthes, Ph. Zt., 72, 1927, 945. (Extraction) Geiger and Hesse, A.J.P., 6, 1834, 320; Blau, A.Ph.A., 52, 1904, 943.

Emetine.—(General) Stewart, Jl. A.Ph.A., 4, 1915, 797. (Structure) Windaus and Hermanns, C.A., 8, 1914, 2776; Carr and Pyman, C.A., 8, 1914, 3418; Karrer, B., 49, 1916, 2057; Pyman, Trans. Ch. Soc., 111, 1917, 419 and 113, 1918, 222; Staub, C.A., 22, 1928, 1977. (Manufacture) Dejussieu, C.A., 8, 1914, 3216. (Pharmacology) Dale, Yearbook, A.Ph.A., 5, 1916, 375 and 7, 1918, 260; Walters and Koch, Jl. Pharmacol. Exp. Therap., 10, 1917, 73.

Emetine Bismuth Iodide.—Anon., Jl. A.M.A., 71, 1918, 2013.

Ipecac.—(History) "X-rayser," Ch. and Dr., 87, 1915, 761; Suppan, Nat. Dr., 45, 1915, 390. (Constituents) Pyman, Jl. Ch. Soc., 105, 1914, 1591; 111, 1917, 419; 113, 1918, 222; Browne, Jl. A.Ph.A., 6, 1917, 1043; Keller, C.A., 22, 1928, 3486. (Pharmacology) Bass and Johns, Jl. A.M.A., 64, 1915, 553; Baumritter, C.A., 23, 1929, 200; Dale, Ph. Jl., 126, 1931, 559. (Preparations) Eschenbrenner, Jl. Soc. Ch. Ind., 50, 1931, 780B.

Gelsemium.—(Constituents) Moore, Jl. Ch. Soc., 97, 1910, 2223 and Jl. Ch. Soc., 99, 1911, 1043; Sayre, A.Ph.A., 58, 1910, 949; J. A.Ph.A., 3, 1914, 314; 4, 1915, 60 and 1458; 8, 1919, 708; Chen and co-workers, Ph. Jl., 127, 1931, 321.

Pareira.—(Constituents) Wiggers, A.J.P., 11, 1839, 352; Faltis, Monatsheft, 33, 1912, 873; Scholtz, Arch. d. Pharm., 250, 1912, 684; Scholtz and Koch, Arch. d. Pharm., 252, 1914, 513; Faltis and Neumann, C.A., 16, 1922, 2866.

Aconite.—(Bibliography) Taylor, Jl. Ind. Eng. Ch., 1, 1907, 549. (Constituents) Groves, Ph. Jl., [2], 8, 1866, 120; Huebschmann, A.J.P., 30, 1858, 399; Schulze and Berger, Arch. Pharm., 262, 1924, 553.

Aconitic Acid.—Pawolleck, A., 178, 1875, 150; Ruhemann and Allhusen, Jl. Ch. Soc., 55, 1894, 9.

Berberis.—(Constituents) Pommerehne, Arch. d. Pharm., 233, 1895, 173.

Colchicum Corm.—(History) Sharp, Ph. Jl., 83, 1909, 5. (Constituents) Pelletiere and Caventou, Jl. de Ph., 8, 1820, 364.

Colchicum Seed.—(History) Sharp, see above. (Constituents) Geiger and Hesse, A.J.P., 6, 1834, 230; Oberlin, Comp. rend., 43, 1856, 1199; Ludwig and Hubler, A.J P., 38, 1866, 105; Rosenwasser, A.J.P., 49, 1877, 435; Hertel, A J.P., 53, 1881, 443; Grimme, Ph. Cent., 61, 1920, 521.

Sanguinaria.—(General) Smith, A.J.P., 3, 1831, 93; Gibb, Ph. Jl., [2], 1, 1860, 454. (Constituents) Thomas, A.J.P., 36, 1864, 134; Hopp, A.J.P., 47, 1875, 193; Koenig, A.J.P., 63, 1891, 457; Schlotterbeck, Am. Ch. Jl., 24, 1900, 249; Danckwortt, Arch. d. Pharm., 250, 1912, 597.

Spigelia.—(History) Wilbert, A.Ph.A., 57, 1909, 1170; Lloyd Library Bulletin, 18, 1911, 82. (Constituents) Stabler, A.Ph.A., 6, 1857, 132; Dudley, A.Ph.A., 30, 1882, 439. (Pharmacology) Sollmann, Jl. A.M.A., 72, 1919, 1228.

Hydrastis.—(History) Lloyd Library Bulletin, 18, 1911, 48; Lewis, A.J.P., 6, 1834, 201. (Cultivation) Lloyd, Ph. Rev., 26, 1908, 138; Stingel, A.J.P., 84, 1912, 299; Langenhan and Hirose, Jl. A.Ph.A., 19, 1930, 340 and 449. (Constituents) Durand, A.J.P., 23, 1851, 112; Mahla, A.J.P., 34, 1862, 141; Hale, A.J.P., 45, 1873, 247; Schmidt and Wilhelm, Arch. d. Pharm., 226, 1888, 330; Gillis and Langenhan, Jl. A.Ph.A., 20, 1931, 210 and 329.

Veratrum.—(Constituents) Bullock, A.J.P., 37, 1865, 321; 38, 1866, 97; 47, 1875, 449; Tobien, A.J.P., 50, 1878, 122; Wright and Luff, A.J.P., 5, 1879, 367; Salzberg, A.J.P., 62, 1890, 493. Viehoever, Keenan and Clevenger, Jl. A.Ph.A., 10, 1921, 581; Stransky, C.A., 15, 1921, 1741.

Cinchona.—(History) Lloyd Library Bulletin, 18, 1911, 17; Anon., Merck's Rept., 37, 1928, 107; Anon., Pract. Dr., 48, April, 1930, 43; Hogstad, *ibid.*, 48, Nov., 1930, 29; Podolsky, *ibid.*, 49, Dec., 1931, 24; Rusby, Jl. A.Ph.A., 20, 1931, 1147; Clark, Merck's Rept., 41, 1932, 140. (Culture) Rosengarten, Pharm. Era, 56, 1923, 537; Howard, Jl. Soc. Ch. Ind., 50, 1931, 189. (Constituents) Pelletiere and Caventou, Jl. de Ph., 7, 1821, 70, 82, 89 and 92; Henry and Delondre, Jl. de Ph., 19, 1833, 623; Pasteur, Jl. de Ph., 24, 1853, 161; Glücksmann, C.A., 11, 1917, 1721. (Tests) von Lingelsheim, C.A., 22, 1928, 2809. (Assays) Dohme, 8th Int. Cong. App. Chem., 17, 1912, 21. (Pharmacology) Chopra and David, C.A., 23, 1929, 2210; Henry, Jl. Soc. Ch. Ind., 49, 1930, 786. (Detannating) Diehl, A.J.P., 40, 1868, 104 (Chinoidine) Rice, Am. Dr., 15, 1885, 46 and 76.

Cinchona Alkaloids.—(Technical use) Jackson, Jl. Ind. Eng. Ch., 22, 1930, 398.

Pomegranate.—(History) Lloyd Library Bulletin, 18, 1911, 44. (Constituents) Tanret, A.J.P., 50, 1878, 389 and 52, 1880, 416.

Aspidosperma.—(General) Holmes, Ph. Jl., 123, 1929, 194. (Yohimbine) Barger and Field, Jl. Ch. Soc., 107, 1915, 1025; Spiegel, Ph. Week., 53, 1916, 448; Raymond-Hamet, C.A., 22, 1928, 4533.

Pilocarpus.—(Constituents) Parodi, A.J.P., 47, 1875, 214; Byasson, A.J.P., 47, 1875, 350; Gerrard, Yearbook Pharm., 1875, 574; Kingsett, Jl. Ch. Soc., 30, 1876, 367; Harnack, A.Ph.A., 35, 1887, 337; Jowett, Jl. Ch. Soc., 77, 1900, 473; Leger and Roques, Dr. Circ., 57, 1913, 744.

Coca.—(History) Sharp, Ph. Jl., 82, 1909, 28, 117 and 184; Lloyd Library Bulletin, 18, 1911, 18. (Culture) Martell, Ph. Cent., 69, 1928, 551. (Constituents) Gaedeke, Arch. d. Pharm., 132, 1855, 141; Niemann, Arch. d. Pharm., 153, 1860, 129 and 291; Loessen, Jl. de Ph., 41, 186, 522. (Action) Koller, through Noves, Dr. Circ., 28, 1884, 165.

Belladonna.—(History) Lloyd Library Bulletin, 18, 1911, 8; Kilmer, Pract. Dr., 42, 1924, 20; Jl. A.Ph.A., 13, 1924, 1131 and 14, 1925, 241; Nat. Dr., 59, 1929, 268; Pract. Dr., 49, Feb., 1931, 16; Jl. A.Ph.A., 21, 1932, 366 and 479. (Constituents) Brandes, A., 1, 1832, 68 and 230. Mein, A., 6, 1833, 67; Geiger and Hesse, A., 7, 1833, 269; Brandes, A., 9, 1834, 122; Lubekind, A.J.P., 13, 1841, 127; Schutte, Arch. Pharm., 229, 1891, 492; Van Itallie, Jl. Pharmacol., 18, 1921, 313; Exler and van Niekerk, *ibid.*, 36, 1929, 411; Todd, C.A., 24, 1930, 2544; Kilmer, Jl. A.Ph.A., 19, 1930, 1315. (Stabilization) Todd, 124, 1930, 94 and 108.

Stramonium.—(History) Meyer, Die Periode der Hexenprocesse, 1882; Holzinger, Zur Naturgeschichte der Hexen, 1883; N. Y. Times, May 13, 1914; Sloane, Virginia Pharmacist, Jan., 1922, 32; Kilmer, A.J.P., 102, 1930, 526. (Constituents) Geiger and Hesse, A.J.P., 6, 1834, 319; Ladenburg, B., 13, 1880, 909; Schmidt, A.J.P., 56, 1884, 440 and 62, 1890, 491; Sivolsbof, Pharm. Era, 53, 1920, 273.

Hyoscyamus.—(Botany and pharmacology) Jl. de ph. et ch., [8], 10, 1929, 143. (Constituents) Ladenburg, B., 13, 1880, 251, 909 and 1549, also A.J.P., 52, 1880, 550.

Scopola.—(History) Lloyd Library Bulletin, 18, 1911, 79; Dunstan, Ph. Jl., [3], 20, 1889, 461. (Constituents) Dunstan and Chaston, Ph. Jl., [3], 20, 1889, 461; Dumez, A.J.P., 86, 1914, 339; Glaser, Arch. Pharm., 266, 1928, 573; Merz, *ibid.*, 270, 1932, 476.

Lobelia.—(History) Lloyd Library Bulletin, 18, 1911, 55; Colhoun, A.J.P., 5, 1833, 300. (Constituents) Procter, A J P., 9, 1837, 98 and 13, 1841, 1; Richardson, A.J.P., 44, 1872, 293; Wieland and co-workers, Jl. Soc. Ch. Ind., 40, 1921, 788A; A., 444, 1925, 40; A., 473, 1929, 83; A., 491, 1931, 14.

Ephedra.—(History and marketing) Chen, Jl. A.Ph.A., 20, 1931, 110. (Constituents) Nagai, Ph. Cent., 29, 1888, 516 and 30, 1889, 188; Chen, Jl. A.Ph.A., 20, 1931, 110 and 339; Kanao, Dr. Circ., 74, Dec., 1930, 35.

Scoparius.—(History) Lloyd Library Bulletin, 18, 1911, 79. (Constituents) Stenhouse, A., 78, 1851, 15; Merck, Ph. Jl., [3], 9, 1879, 1060; Perkin, A.Ph.A., 47, 1899, 764; Valeur, Chem. News, 117, 1918, 340; Herzig, C.A., 13, 1919, 421; Hemmelmayr and Strehley, C.A., 21, 1927, 575.

Chelidonium.—(Constituents) Gadamer, Arch. Pharm., 257, 1919, 298; Apoth. Zt., 39, 1924, 1569; Bruchhausen and Bersch, B., 63B, 1930, 2520; Spaeth and Kuffner, B., 64B, 1931, 370. (Pharmacology) Hanzlik, Jl. A.M.A., 75, 1920, 1324.

Conium.—(History) Griffith, A.J.P., 6, 1835, 267. (Constituents) Giesecke, A.J.P., 1, April, 1829, 76; Geiger, Ch. Cent., 3, 1832, 1; Wertheim, A., 100, 1856, 328; Smith, A.J.P., 40, 1868, 459; Stoddart, Ph. Jl., [3], 1, 1871, 843.

Nux Vomica.—(History) Tschirch, Ph. Jl., 101, 1918, 120; Schelenz, Jl. ph. ch., 18, 1918, 63; Roddis, Ph. Era, 66, 1929, 298. (Constituents) Pelletiere and Caventou, Jl. de Ph., 5, 1819, 145; Henry, A.J.P., 7, 1835, 233; Dunstan and Short, A.J.P., 56, 1884, 431; Schroeder, Arch. d. Pharm., 250, 1912, 398; Azadian, Sch. Wsch. f. Ch. u. Ph., 51, 1913, 761; Schaefer, Jl. A.Ph.A., 3, 1914, 1677; Heiduschka and Wallenreuter, Arch. Pharm., 250, 1912, 398 and 401; 253, 1915, 143; Watt and Angus, C.A., 10, 1916, 1404; Hobart, Ph. Jl., 112, 1924, 670; Wieland and Oertel, C.A., 23, 1929, 3474; Ruickoldt, C.A., 25, 1931, 3391; Warnat, C.A., 26, 1932, 731.

Physostigma.—(History) Sharp, Ph. Jl., 96, 1916, 619. (Constituents) Salway, Jl. Ch. Soc., 99, 1911, 2148; Polonovski, Ph. Jl., 95, 1915, 513; Ph. Week., 54, 1917, 1289; C.A., 12, 1918, 40; Heiduschka and Gloth, Arch. Pharm., 253, 1915, 415; Cattelain, Jl. de ph. et ch., [8], 1, 1925, 59; Windaus and Brunken, C.A., 19, 1925, 473.

Staphisagria.—(Constituents) Lassaigne and Feneulle, Jl. de Ph., 6, 1820, 366; Kara Stojanow, A.J.P., 62, 1890, 394.

Sabadilla.—Wright and Luff, A.J.P., 50, 1878, 489.

Ergot.—(History) Tschirch, C.A., 11, 1917, 2531; Barger, Ph. Jl., 105, 1920, 470. (Culture) McCrea, Jl. A.Ph.A., 20, 1931, 270. (Constituents) Barger and co-workers, Ph. Jl., 77, 257 and 84, 1910, 710 and 127, 1932, 420; Jl. Soc. Ch. Ind., 50, 1931, 178; Jl. Ch. Soc., 91, 1907, 337 and 95, 1909, 1123; Tanret, Comp. rend., 81, 1875, 896 and 86, 1878, 888; Wenzel, A.J.P., 36, 1864, 192 and 82, 1910, 410; Rathje, Arch. d. Pharm., 246, 1908, 696; Kobert, Ph. Cent., 27, 1886, 597 and Ph. Zt., 52, 1908, 839; Freeborn, Ph. Jl., 88, 1912, 568; Crawford, A.J.P., 83, 1911, 147; Tschirch, C.A., 16, 1922, 2386; Stoll, Jl. Soc. Ch. Ind., 41, 1922, 914A; Eagles and Johnson, Jl. Am. Ch. Soc., 49, 1927, 575 and 50, 1928, 1386; Tainter, C.A., 22, 1928, 2616; Behre and Benedict, C.A., 23, 1929, 2733; Stoll, Pract. Dr., 47, Sept., 1929, 33 and 49, March, 1931, 33; Smith and Timmis, Jl. Ch. Soc., 1930, 1390; 1931, 1888; 1932, 1543; Matthes and Kürscher, Arch. Pharm., 269, 1931, 88; Moir, Ph. Jl., 128, 1932, 510; Schlemmer, Arch. Pharm., 270, 1932, 15; Kindler and Peschke, *ibid.*, 270, 1932, 341; Hill, Ph. Jl., 128, 1932, 83; Burn, *ibid.*, 134, 1935, 357; Thompson, Science, 81, 1935, 636; Dale, *ibid.*, 82, 1935, 101; Kharasch, *et al.*, Science, 83, 1936, 206; Anon., *ibid.*, 83, 1936, 296. (Standardization) Tschirch, Jl. Soc. Ch. Ind., 45, 1926, 848B; Rusby, Jl. A.Ph.A., 18, 1929, 1125; Swanson, *ibid.*, 18, 1929, 1127; Smith, C.A., 24, 1930, 4118. (Preservation) Schindelmeyer, A.Ph.A., 58, 1910, 157; Wood, A.J.P., 83, 1911, 172; Anon., Am. Dr., 56, 1910, 166. (Pharmacology) Lieb, C.A., 1914, 1831; Hanzlik, Jl. A.M.A., 72, 1919, 577; Rothlin, C.A., 18, 1924, 2759 and 23, 1929, 4267; Burn, C.A., 24, 1930, 2184; Thompson, Jl. A.Ph.A., 18, 1929, 1106; 19, 1930, 11, 104, 221, 436 and 705; Wokes, Ph. Jl., 125, 1932, 203.

Opium.—(History) Billiger, Ph. Jl., [3], 7, 1876, 452; Wilbert, Jl. A.Ph.A., 5, 1916, 688; Rosenthaler, Schw. Ap. Zt., 58, 1920, 409; Jermstad, *ibid.*, 57, 1919, 387 and 399; 59, 1921, 26, 34, 50, 69 and 85. (Collection) Heinicke, West. Dr., 46, 1924, 76. (Bibliography) Schmidt, Pharm. Era, 46, 1913, 593. (Constituents) Robiquet, A., 5, 1832, 82; Couerbe, A.J.P., 4, 1832, 262; Pelletier, A J.P., 5, 1833, 150 and 8, 1836, 62; O'-Shaugnessy, A.J.P., 12, 1840, 138; Thoms and Pietrulla, Ph. Zt., 65, 1920, 753; Wieland and Kotake, Jl. Soc. Ch. Ind., 44, 1925, 969B.

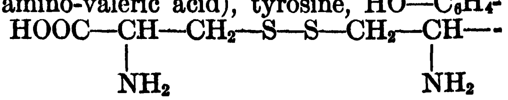
Deodorized Opium.—Robiquet, Jl. de ph. ch., 8, 1822, 438; Ebert, A.J.P., 39, 1867, 193 and 74, 1902, 157; Anon., D.-A. Ap. Zt., 3, 1883, 751.

CHAPTER LI

THE PROTEINS

The proteins, or albuminoids, represent a group of complex organic substances, containing hydrogen, oxygen, nitrogen, and sulfur. The chemistry of these bodies is so complex that very little is known of their exact composition. Different proteids, however, possess different proportions of the elements above mentioned, and vary in constitution from simpler bodies, like protamine, to very complex substances, which can be split into many different chemicals.

All proteins seem based upon the urea molecule, to which is attached a number of other bodies. Among these bodies, constituting part of the protein molecule, may be mentioned sulfurated compounds, carbohydrate derivatives (like levulinic acid), phosphoric acid, and notably a series of amino-acids such as glycine (or glycocoll, p. 671); valine (p. 687), leucine $(CH_3)_2CH—CH_2CH(NH_2)COOH$, lysine, norvaline $(CH_3)_2CH—CH(NH_2)CH(NH_2)COOH$ (an amino-valeric acid), tyrosine, $HO—C_6H_4—CH_2CH(NH_2)COOH$, cystine, $HOOC—\underset{NH_2}{\underset{|}{CH}}—CH_2—S—S—CH_2—\underset{NH_2}{\underset{|}{CH}}—COOH$, histidine and histamine.



The foregoing statements indicate that the molecular weight of the proteins must be very large. Svedberg finds the molecular weight of egg albumin is about 34,500. He also expresses the opinion that the molecular weight of even more complex bodies are multiples of the above figures. Thus to amandin (from almonds) and to edestin (from rye) he ascribes the molecular weight 208,000 to 212,000 (34,500 × 6). Casein, on the other hand, appears to have a molecular weight as high as 375,000.

The following is a modern classification of proteins:

I. **Holoproteins.**—Proteins yielding upon hydrolysis, amino-acids and ammonia.

- Protamines.—Simplest form of albumin. Example, salmine ($C_{30}H_{57}N_{17}O_6$), found in salmon spawn.
- Histones.—More complex bodies isolated from blood corpuscles. Precipitated by ammonia.
- Albumins.—Soluble in water, diluted acids, alkalis, saturated solution of sodium chloride. Coagulated by heat. Contain glycocoll. Examples, serum-albumin, egg-albumin, milk-albumin, and the albumin of seeds.
- Globulins.—Insoluble in water, soluble in dilute solution of sodium chloride. Coagulate on boiling. Do not contain glycocoll. Examples, myosin (from lean meat), fibrinogen (the blood constituent that clots), serum globulin, and vegetable globulins.
- Glutenins.—Wheat proteins; soluble in dilute alkalis.
- Gliadins.—Simple proteins derived from gluten.
- Scleroproteins.—Horny material like gelatin.
- Keratins.—Proteins from horns, hoofs and fingernails.

II. **Heteroproteins.**—Proteids yielding upon hydrolysis amino-acids, ammonia and nonprotein substances.

- Phosphoproteids.—Conjugated proteids consisting of a simple protein plus a phosphorus compound other than nucleic acid or lecithin.
- Nucleoproteids.—Those isolated from yeast cells; derivatives of the nucleic acids.
- Glucoproteids.—Insoluble in water; soluble in 60 per cent alcohol. Example, mucin.
- Chromoproteids.—Those having marked colors, such as hemoglobin.

Among the *protein derivatives* may be cited:

- Metaproteins.—Insoluble in water, soluble in acids and alkalis. Example, syntonin.
- Proteoses.—Partly soluble in water. Products of digestion of albumin with vegetable enzymes like papain. Found in many seeds.
- Peptones.—Perfectly soluble in water. Not precipitated by sodium chloride.
- Polypeptides.—Mostly synthetic substances; some products of hydrolysis of proteins.

Serum-albumin is of particular interest to us inasmuch as, in the derangement of the human system producing the complaint called Bright's disease, the serum-albumin of the blood passes through the diseased kidney tissue and appears in the urine. The significance of the presence of albumin in the urine is beyond the limits of this book, and for further particulars on this interesting and important subject the reader is referred to standard works on urinary analysis.

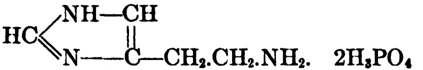
Egg-albumin is of interest as an important foodstuff. While ordinary egg-albumin is difficult to crystallize, its crystallization has been accomplished by Hopkins. Egg-albumin combines with iron salts to form iron albuminate, which dissolves in dilute alkali. The soluble (scale) form of this chemical is made with sodium citrate.

Coagulated egg-albumin, digested with pepsin and acid, dissolves with the formation of *peptone*, which has the same percentage composition as pepsin. This is a basis of the U.S.P. pepsin assay. Most commercial peptones are made from lean beef instead of from eggs. Peptone, like egg-albumin, forms a soluble iron salt—iron peptonate.

HISTAMINÆ PHOSPHAS—Histamine Phosphate

(Histamin. Phos.—Histamine Acid Phosphate)

$C_5H_9N_3.2H_3PO_4$



Molecular weight, 307.18

A phosphate of β-iminazolylethylamine.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Colorless prismatic crystals, odorless; stable in air; soluble in 4 parts of water at 25° C.; more soluble in hot water; melts at about 130° C. For details, see U.S.P., p. 184.

For *tests for identity* and for *impurity* (excess of moisture), see U.S.P., p. 184.

Remarks.—This new official chemical is used as a diagnostic test in differentiating between pernicious and secondary anemia. It is administered by subcutaneous injection.

LIQUOR HISTAMINÆ PHOSPHATIS—Solution of Histamine Phosphate

(Liq. Histam. Phos.—Solution of Histamine Acid Phosphate)

Condensed Recipe.

Dissolve 1 Gm. histamine phosphate in sufficient water to make 1000 cc., filtering if necessary to make a clear solution.

Storage.—Preserve in small, well-filled bottles or in ampuls.

Remarks.—This solution is of the strength usually employed for diagnostic purposes. The Pharmacopoeia permits the addition of a suitable preservative as provided on page 7, U.S.P. XI. In addition to the use described above under Histamine, a drop of this solution may also be used as an interdermal diagnostic test of certain diseases with decreased circulation, such as Raynaud's disease, arteriosclerosis, etc.

Dose.—0.3 cc. (5 minims) by parenteral injection.

ALBUMINI TANNAS—Albumin Tannate

(Album. Tan.—Albutannin)

A compound of albumin and tannic acid.

Storage.—Preserve in well-closed containers and protected from light.

Summarized Description.

Yellowish-white odorless powder; almost insoluble in water, alcohol, chloroform and ether; decomposed by solutions of alkalis. For details, see U.S.P., p. 44.

For *tests for identity* and for *impurities* (free acid, soluble matter), see U.S.P., p. 44.

Remarks.—*Albutannin* is obtained by precipitating a solution of egg-albumin with a solution of tannin. It is a yellowish-white powder, that is almost insoluble in water. It is an astringent that acts in the alkaline fluids of the intestines rather than in the acid fluid of the stomach.

Dose.—2 Gm. (30 grains).

Peptonized Iron (N.F. VI) is a compound of iron oxide and peptone, rendered soluble by the presence of sodium citrate. It is a constituent of *solution of peptonized iron,* N.F. (p. 213) and of *solution of peptonized iron and manganese* N.F. (p. 213).

Phytoalbumin is of pharmaceutic interest merely because it makes up the larger bulk of horny seeds—an official example being the albumin of nux vomica.

Globulin is of passing interest because one form of it is a constituent of albuminous urine, and differs from serum albumin by being precipitated by magnesium sulfate.

Fibrinogen is an albuminoid of the blood, the clotting of which is caused by the conversion of the substance into fibrin.

Vitellin is the albuminoid found in yolk of egg.

Syntonin is acid albumin, and can be made by boiling egg-albumin with nitric acid. It is here mentioned because its formation often misleads the tyro in urinary analysis in the nitric acid test. If nitric acid be added to urine containing albumin, the latter coagulates and precipitates. If too much acid is added, syntonin is formed, and no precipitation occurs.

Legumin is found in the seed of the *Leguminosæ.* It is soluble in diluted alkali.

Casein is the chief albuminoid of milk, from which it can be separated by means of rennet, acids, and some salts, such as the alums. It has many industrial uses in addition to its food value.

GELATINUM—Gelatin

(Gelat.)

A product obtained by the partial hydrolysis of collagen, derived from the skin, white connective tissue, and bones of animals.

Summarized Description.

Amorphous solid in sheets or flakes, in ground or shredded form or in coarse or fine powder; colorless or slightly yellow; slight characteristic odor or taste; stable in air when dry, decomposes when moist; insoluble in cold water, but softens with 5 to 10 parts of that fluid; soluble in hot water, acetic acid or in a mixture of glycerin and water, insoluble in alcohol, chloroform, ether, benzene, carbon disulfide or in fixed or volatile oils; a hot solution (1 in 40) forms a jelly on cooling. For details, see U.S.P., p. 176.

For *tests for identity* and for *impurities* (sulfur dioxide, heavy metals, arsenic), see U.S.P., p. 177.

Remarks.—Gelatin is a mixture of a large number of nitrogenous substances, such as glycocoll, alanine, leucine, glutannic acid, histidine, etc. It is prepared by boiling bones in water under pressure (as in a boiler), skimming the solution of gelatin to remove fat, and clarifying if necessary. On cooling the gelatin solidifies, and this is cut into cakes and dried on fish nets. This explains the netted marking on the best quality of the sheet gelatin.

Glue is an impure gelatin made by digesting all kinds of gelatinous animal refuse—hide, horns, hoofs, as well as bones—by the process just given.

Gelatin is not soluble in cold water, but swells therein to form a jelly in which there is a network of protein molecules enclosing the adsorbed liquid. It dissolves in boiling water, and is not precipitated from this solution by nitric acid nor by potassium ferrocyanide, as is egg-albumin. The precipitate formed when its solution is treated with tannin is similar to leather (p. 162). Its jelly is made impervious to moisture by treatment with potassium dichromate. Formaldehyde acts in the same way, and these two chemicals are now used for tanning finer grades of leather. The present Pharmacopœia directs that gelatin contain no more than $4/1000$ of 1 per cent of sulfur dioxide and that gelatin capsules contain no more than $15/100$ of 1 per cent of that bleaching agent. The official test consists in treating the gelatin with phosphoric acid and sodium bicarbonate, distilling the sulfur dioxide into tenth-normal iodine V.S. (which oxidizes the H_2SO_3 into H_2SO_4) and then precipitating the resulting sulfate with barium chloride.

GELATINUM GLYCERINATUM—Glycerinated Gelatin

(Gelat. Glycerin.)

Storage.—Preserve in well-closed containers.

Condensed Recipe.

Soak 100 Gm. gelatin in water; drain off the surplus water; add 100 Gm. glycerin and heat on a water-bath until the gelatin is dissolved. Strain and then heat until mixture weighs 200 Gm. For details, see U.S.P., p. 177.

Remarks.—The faintly straw-colored transparent jelly thus produced is used as a suppository base (p. 354), although, from what has been said concerning the formation of leather from gelatin, it is clear that this base should not be used in making tannin suppositories. It is important that all the water be driven off in making the mass, as provided by the Pharmacopœia, for if any remains, the mass grows moldy and turns dark brown.

Gelatin Solutions (10 per cent) are used somewhat in Europe by hypodermic injection as hemostatics. Of course such solutions must be carefully sterilized.

Keratin has already been mentioned as a coating for enteric pills (p. 339). It is a scleroprotein resembling gelatin and is obtained from horn and feathers and hair. It contains 7 to 8 per cent of cystine (p. 948). Because of its relation to the hair Zuntz seriously suggests its internal administration (after hydrolysis) as a hair grower.

Nuclein is the albuminoid of the cell nucleus, that center of activity of the living cell.

Hemoglobin is an iron-bearing constituent of the blood, to which it transmits its red color. By treating defibrinated blood with acidulated pepsin and exactly neutralizing with sodium carbonate there is precipitated *Hematin,* which has been recommended as a remedy for anemia, since it contains iron in easily assimilable form. Its crystalline hydrochloric acid compound is called *hemin.* This is closely related to ætiophyllin, a chlorophyll derivative. (See p. 881.)

ENZYMES

Enzymes are complex bodies presumably protein derivatives although some investigators claim that their protein properties are due to admixed impurities. Because of their colloidal character, the separation of the pure enzymes is well-nigh impossible and as Czapek says "we know enzymes only by their actions." From this standpoint, we may regard enzymes as insoluble colloids, which are energetically adsorbed (p. 156) by such agents as infusorial earth, kaolin or even by filter paper. That enzyme action does not proceed along the routine lines of molecular proportions seems shown by their extreme activity. Thus, 1 part of invertase hydrolyzes 200,000 parts of sugar, while 1 part of rennin is capable of coagulating 800,000 times its own weight of casein in a sample of milk. Enzymes are therefore to be regarded as "the catalytic agents of the living cells" and are found both in animal and in vegetable tissue. Czapek classifies them according to their action as follows:

I. *Hydrolyzing enzymes* (Hydrolases).
  (*a*) Hydrolyse carbohydrates (carbohydrases). Examples, invertase, diastase, maltase, lactase, amylase, pectase, etc.
  (*b*) Hydrolyse glucosides. Examples, emulsin, myrosin, etc.
  (*c*) Hydrolyse fats (lipases).
  (*d*) Hydrolyse proteins. (Proteolytic enzymes or proteases.) Examples, pepsin, trypsin, etc.

II. *Enzymes, splitting off CO_2 from bodies without addition of oxygen.*
(*a*) Those acting on hexoses. Example, zymase, found in yeast.
(*b*) Those acting on amino-bodies. Example, urease.

III. *Oxydases.* Some of these oxidize alcohols and aldehydes to acids (such as the enzymes in mother of vinegar, p. 668) while many of them oxidize phenols and other plant substances.

IV. *Reducing enzymes.* (Reductases.)

V. *Lactic acid enzymes.* (Lactases.)

Most enzymes are rendered inactive at 60° C. and all are destroyed when heated to 100° C. Alcohol usually lessens enzyme action; while acids frequently increase their activity. Some enzymes exert a synthetic action as is shown in the synthesis of arbutin (p. 713).

Among the important enzymes or enzyme mixtures are the following:

Amygdalase, an enzyme in bitter almond, presumably a constituent of what we commonly call emulsin.

Diastasum (U.S.P. IX), or *Diastase,* is the mixture of enzymes, obtained by macerating malt with cold water, and then pouring the filtered infusion into double the amount of strong alcohol. Taka diastase is prepared by treating wheat bran with a peculiar fungus, called in Japan "moyashi," extracting the diastase thus formed with water, and precipitating with alcohol. Diastase converts starch into dextrin and maltase, and is, therefore, used in starchy indigestion *Dose.*—500 mg. (9 grains).

Emulsin is the enzyme of bitter almond (p. 795).

Invertase is an enzyme found in yeast (p. 957).

Linase is the hydrolyzing enzyme of flaxseed and of other plants of the Flax family.

Lipases, or fat-splitting enzymes, are found in a large number of plants. Among these may be cited the lipase of the castor oil bean, which is actually employed in one method of manufacturing glycerin (p. 678).

Myrosin is the enzyme found in black mustard (p. 754).

PANCREATINUM—Pancreatin

(Pancreat.)

Pancreatin is a substance containing enzymes, principally amylopsin, trypsin, and steapsin, obtained from the fresh pancreas of the hog, *Sus scrofa* var. *domesticus* Gray (Fam. *Suidæ*) or of the ox, *Bos taurus* Linné (Fam. *Bovidæ*).

It converts not less than 25 times its weight of starch into soluble carbohydrates and not less than 25 times its weight of casein into proteoses. Pancreatin of a higher digestive power may be brought to this standard by admixture with lactose.

Storage.—Preserve in air-tight containers in a cool place.

Summarized Description.

Cream-colored amorphous powder; faint but not offensive odor; slowly and completely soluble in water; insoluble in alcohol; converts proteins into proteoses and starch in dextrins and sugars; active in faintly alkaline media; strongly acid or alkaline solutions are inert.

For *tests for identity* and for *impurity* (fat), see U.S.P., p. 275.

For *assays for starch digestive power* and for *casein digestive power,* see U.S.P., pp. 275 and 276.

Composition.—The enzymes, amylopsin, myopsin, trypsin, and *steapsin.* Trypsin and myopsin digest albumin, amylopsin hydrolyses starch, while steapsin emulsifies fats. Northrop has isolated from commercial preparations of trypsin protein crystals which are ten times more active as a digestant than the original source.

Extraction.—The minced pancreas is macerated for some time with water containing enough chloroform to prevent putrefaction. The liquid is then expressed from the residue, is filtered, and rapidly evaporated at a temperature not exceeding 45° C.

Remarks.—One test for pancreatin is the estimation of its peptonizing power; that is, 0.3 Gm. of pancreatin and 1.2 Gm. of sodium bicarbonate should be capable of converting the albumin of 500 cc. cows' milk into peptone, which is not coagulated by acetic acid. Not only is this process used as a test, but the *peptonized milk* is itself sometimes used as a diet where the stomach cannot tolerate the natural albumin of milk.

One of the two official assays of pancreatin is based on its ability to convert starch into dextrin and maltose; the requirements being that 1 part of pancreatin should be able to transform at least 25 times its weight of starch.

The second official assay of pancreatin is based upon the fact that 1 part of the official product should convert 25 times its weight of casein into proteoses.

While pepsin acts in an acid medium, pancreatin is of value only when combined with mild alkalis, and this emphasizes the absurdity of prescribing these two substances in combination, a medium which will develop the activity of pepsin rendering pancreatin inert.

Pepsin and pancreatin are of value in dyspepsia, both acting as food digestants; their natural function in the animal economy. The two differ, however, as to the kind of food each digests, pepsin digesting albuminoid matter in the stomach, while pancreatin digests albuminoids, starch, and fat in the intestines. To be effective, pancreatin should be administered only in enteric pills. It is a constituent of *peptonizing powder* N.F. (p. 317).

Dose.—500 mg. (8 grains).

Papain is the enzyme obtained from the milk juice of *Carica papaya,* and has been recommended as a general digestant and for dissolving the diphtheritic membrane.

PEPSINUM—Pepsin

(Pepsin.)

Pepsin is a substance containing a proteolytic enzyme obtained from the glandular layer of the fresh stomach of the hog, *Sus scrofa* var. *domesticus* Gray (Fam. *Suidæ*).

Pepsin, when assayed as herein directed, digests not less than 3000 and not more than 3500 times its weight of egg albumen. A pepsin of higher digestive power may be reduced to the official standard by admixture with a pepsin of lower power or with lactose.

Storage.—Preserve in well-closed containers in a cool place.

Summarized Description.

Lustrous, white or pale yellow, transparent or translucent scales, or grains, or spongy masses, or white or cream-colored amorphous powder; free from offensive odor; only slightly hygroscopic; forms an opalescent solution with about 50 parts of water; almost insoluble in alcohol, chloroform or ether; incompatible with alkalis, alkaline earths or alkali carbonates. For details, see U.S.P., p. 279.

For *assay,* see U.S.P., p. 279.

Extraction.—The mucous membrane of the hog's stomach is treated with water acidulated with hydrochloric acid at a temperature of 38° to 45° C. until the entire mass is fluid, chloroform or sulfurous acid being used to prevent putrefaction, and the liquid allowed to stand over night, whereupon the fluid portion is strained from the sediment, evaporated in vacuo to the consistence of a syrup, which is scaled on plates of glass.

In order to free it from peptone, pepsin is sometimes precipitated from the acidulated solution by saturating the latter with sodium sulfate, redissolving the precipitate in diluted acid and finally separating the sodium sulfate from the pepsin by dialysis.

Remarks.—Northrop has prepared pepsin in crystalline form of such purity that one part of the crystals is capable of digesting 20,000 times its own weight of coagulated albumin. Even in this concentration, pepsin indicates its protein character. Commercial pepsin (1 : 3000) contains foreign matter, such as mucus, peptones, and syntonin.

While it has been long known that pepsin acts as a digestant only in acid solution, it acts well only in hydrochloric and phosphoric acid solution and then only when of proper acid strength. Thus pepsin solutions keep properly only when the acid concentration is not less than 0.05 per cent nor more than 0.1 per cent HCl. Pepsin is rendered inert or is decomposed by alkalis (including sodium bicarbonate) and by bismuth subcarbonate and subnitrate. Pepsin and pancreatin should not be prescribed together as mentioned on page 227. Whether alcohol markedly affects its action is a matter of controversy.

Incompatibilities.—See prescription No. 17 in Chapter LIX.

Medical Properties.—Pepsin is a valuable aid to digestion. While there are no preparations of pepsin recognized in the Pharmacopœia, the National Formulary gives recipes for *saccharated pepsin* (pepsin, 10 per cent, sugar of milk, 90 per cent) and for five elixirs containing pepsin, including *compound elixir of pepsin,* popularly known as *compound digestive elixir* (p. 227).

Dose.—500 mg. (8 grains).

Rennin (N.F. VI) is the milk-curdling enzyme obtained from the stomach of the calf. Balls considers it to be merely a modification of pepsin. It is a constituent of *elixir of pepsin and rennin* (p. 230).

Urease is an enzyme found in soy bean (p. 736). It has the property of converting urea into ammonium carbonate and is now largely used for this reason in the quantitative determination of urea in urine. Mack and Villars have found that by regulating the concentration and temperature of the solution, the reaction may be reversed and urea may be synthesized from ammonium carbonate. Urease has been produced in pure crystalline form by Sumner.

Zymase is an enzyme found in yeast (p. 957).

TOXINS

Toxins are bodies, presumably proteins, that resemble enzymes in many ways. They are adsorbed even as are enzymes and have their activity lessened by those agents affecting enzyme action. As described later, the bacteria of disease supply to the blood destructive toxins which are intensely poisonous and which transmit to the victim the symptoms characterizing the disease.

In addition to these disease toxins, phytotoxins (*toxalbumins*) or similar bodies of vegetable origin are known. Among these may be cited *ricin,* the toxin of the castor oil bean; *abrin,* from jequirity seed; among the animal toxins (other than bacteriological) may be cited *bufotoxin,* from the toad, *Bufo vulgaris* and *snake venom,* the cause of death from snake bite. From fresh snake venom, there are now prepared antitoxins, by methods somewhat similar to that employed in preparing diphtheria antitoxin (see p. 978); *animirtin* or the toad stool toxin; and the *aspergillus* or mold toxin, which is supposed to cause pellagra. It is also claimed that hay fever is due to certain pollen toxins while the poisonous quality of the sting of bees and other insects is now supposed to be due to toxins rather than to formic acid (p. 651).

VITAMINS

The term "vitamine" was coined by Funk to designate the principle found in rice polishings that relieved the disease (beriberi) produced by use of polished rice as an almost exclusive diet. Specialists in oriental diseases had previously noted the connection between beriberi and the persistent eating of uncoated (polished) rice and after Funk's discovery of the vitamin in rice bran, other dietetic experts found that other

VITAMIN TABLE

Katharine H. Coward (Ph. Jl., 131, 1933, 293)

Name.	Occurrence.	Properties.	Effect of cooking.	Effect of deficiency on human body.
A	Halibut liver oil, cod liver oil, mammalian liver oils, milk, butter, eggs, leafy vegetables and salads, carrots, some fruits (orange).	Soluble in fat-solvents, easily oxidised, heat stable in absence of air.	Destruction dependent on chances of oxidation.	Cessation of growth when body reserves are exhausted. Keratinization of epithelium of eyelids, respiratory tract, vagina, etc.
B_1	Dried yeast, embryos of seeds, most leafy vegetables, organs and muscles of many animals, milk (little).	Soluble in water, heat labile especially in alkaline solution.	Easily destroyed.	Cessation of growth. Development of beriberi.
B_2	Dried yeast, milk, egg-white, most leafy vegetables, organs and muscles of many animals.	Soluble in water, more stable to heat than B_1, but not entirely so.	Less easily destroyed than B_1.	Cessation of growth. Development of pellagra (probably).
B_3	Wheat, air-dried yeast.	Soluble in water, thermolabile.	Easily destroyed.	So far only shown to be necessary for the pigeon's maintenance of weight.
B_4	Yeast.	Soluble in water, thermolabile.	Easily destroyed.	So far only shown to be necessary for the rat which, without it, develops muscular weakness, spastic gait, humped back, etc.
B_5	Yeast, whole wheat.	Soluble in water, stable to heat and alkali.	Not destroyed.	So far only shown to be necessary for the pigeon's maintenance of weight.
Y (Possibly allied with the B vitamin.)	Yeast.	Soluble in water, stable to heat and alkali.	Not destroyed.	So far only shown to be necessary for growth of the rat.
C	Practically all fresh fruit and vegetables, germinated peas and beans.	Soluble in water, easily oxidized though fairly stable at *p*H 2.2 (the acidity of lemon juice).	Very easily destroyed.	Development of scurvy. Changes in the dentine of teeth.
D	Cod liver oil and some other fish-liver oils, butter and milk (little).	Soluble in fat-solvents, more stable than vitamin A though not completely so.	Slight destruction.	Retardation of growth. Development of rickets. Unsound formation of teeth.
E	Wheat germ, green vegetables and salads.	Soluble in fat-solvents, heat stable, not oxidized by exposure to air.	Not destroyed.	So far only shown to be necessary for rats and mice and possibly hens Retardation of growth. Degeneration of seminal vesicles in males. Resorption of fetuses in females.

types of malnutrition were due to vitamin deficiency and other forms of vitamins have been discovered. It will be noted that Funk called these substances "vitamines" since he first thought that the substance isolated from rice polishings was a nitrogenous base. As it is now known that these substances are not alkaloids, it is deemed best, to drop the "e" and to call them *vitamins*.

While the original vitamin concentrates represented products in which the vitamin had been absorbed by hydrous aluminum silicate or Lloyd's reagent (p. 549) the oil-soluble vitamin A is now furnished in oleaginous form while vitamins B, C and D have been obtained as pure crystals.

As to *sources* of vitamins, we have already spoken of rice polishings. Vegetables, such as spinach and cabbage; fruit, such as orange and lemon juice; fats, notably cod liver oil; and lastly yeast in which vitamins are present in large quantity; contain these substances and in a well-balanced diet, such food stuffs as have just been mentioned furnish the factor (the vitamin) preventing malnutrition and the diseases that follow in its wake. (See lemon juice, p. 689; cod liver oil, p. 736.)

The following types of vitamins have been identified:

Vitamin A.—Fat-soluble, abundant in the oil of the liver of cod and other fishes. Karrer finds that it is a derivative of carotene (p. 882) and that its structure closely resembles ionone (p. 831).

Vitamin B.—Antineuritic. This is Funk's original vitamin. The pure vitamin is said by Windaus to have the formula $C_{12}H_{17}N_3OS$, while Ohdake inclines to the formula $C_{12}H_{16}N_4SO_2$. Williams and Waterman (1934) succeeded in isolating this vitamin from rice polishings in pure crystalline form.

Vitamin C.—Antiscorbutic. Abundant in orange, lemon and cabbage juice. While Rygh (1931) believed this vitamin to be a narcotine derivative, Szent Gyorgyi and others incline to the belief that it is a derivative of ascorbic acid. Vitamin C is spoken of as ascorbic acid or cevitamic acid.

Vitamin D.—Antirachitic. The second vitamin constituent of cod liver oil. This vitamin was obtained in crystalline form in 1932 by Windaus, who ascribes to it the formula $C_{27}H_{42}O$. It is probably stereoisomeric with ergosterol (pp. 747, 941 and below) which in turn is closely allied to cholesterol (p. 747). A highly purified form of this vitamin is now on the market under the trade name, *Calciferol.*

Steenbock and others have found that treatment of ergosterol with ultraviolet light causes the sterol to assume high antirachitic value. There are many "irradiated ergosterol" products now upon the market.

Vitamin E.—Antisterility vitamin obtained from the wheat germ. See appended table.

Vitamin G.—Also called "vitamin B_2." The antipellagric vitamin found along with vitamin B in rice polishings and also largely in yeast.

Much work has been performed in the evaluation and standardization of vitamin preparations. U.S.P. XI provides vitamin assays for cod liver oil. Coward (1933) condenses essential vitamin information in the table on page 956.

LIQUOR ERGOSTEROLIS IRRADIATI—Solution of Irradiated Ergosterol

(Liq. Ergosterol. Irrad. Viosterol in Oil)

A solution of ergosterol in an edible vegetable oil, activated by irradiation with ultraviolet rays. Solution of Irradiated Ergosterol contains in each Gm. not less than 10,000 U.S.P. units of vitamin D.

Storage.—Preserve in small, well-stoppered bottles, in a cool place.

Summarized Description.

Clear colorless oily liquid; almost odorless; bland taste; slightly soluble in alcohol; miscible with ether, chloroform, benzene and petroleum benzin. For details, see U.S.P., p. 208.

For *tests for identity* and for *assay*, see U.S.P., p. 208.

Remarks.—This is irradiated ergosterol prepared by the Steenbock process. It is standardized to 10,000 U.S.P. units of vitamin D.

Dose.—0.3 cc. (5 minims).

Yeast (N.F. V) as already explained (p. 655) consists of myriads of microscopic plants of the genus, *Saccharomyces,* employed in the fermentation of starchy or saccharine material into alcohol. Ordinary yeast contains about 80 per cent of water. This water can be removed and the semisolid product, *yeast cake,* is largely used in baking.

Yeast contains water, nitrogenous matter (glycocoll, alanine, valine, leucine, proline, aspartic, nucleic and glutamic acids, tyrosine, etc.), enzymes (zymase, invertase, maltase, etc.), sterols (ergosterol and zymosterol), vitamins and fatty matter.

During the Great War, the Teutons attempted to utilize dry yeast as a food. Used fifty years ago in domestic medicine, it has recently come into therapeutic vogue because of its vitamin content.

Flesh is a combination of fibrous tissue with blood, albuminoids, and a host of other substances, such as the urea derivatives, sarcin, and carnin.

Meat preparations used for invalid diet are a part of the stock of the modern drug store, hence a few words concerning these are in place. Of these meat products the only ones of real nutritive value are *meat juices*, made by expressing the juice from a slightly broiled steak. These juices decompose as rapidly as does meat itself, hence must be either fortified by preservatives or dispensed in a perfectly fresh condition. The writer knows of several progressive pharmacists who have built up a large trade in meat juice, preparing same fresh every day.

Beef tea is made by digesting finely chopped meat with warm water and straining.

Beef extracts represent beef tea evaporated in vacuo—being administered redissolved in warm water. Both of these products are practically devoid of nutritive qualities, its stimulating action being due to the sarcin and carnin they contain, these bodies acting similarly to their allied body, caffeine. One authority has claimed that "beef tea" has little more nutritive action than has urine.

Milk is casein emulsion of fat (butter), containing milk sugar and inorganic salts.

Lac Vaccinum (N.F. VI), cows' milk, is the fresh unpasteurized or pasteurized milk of the domestic cow, *Bos taurus* Linné (Fam. *Bovidæ*), without modification, complying with the legal standards of the state or community in which it is sold.

When milk is treated with yeast, the milk sugar ferments to lactic acid, and if the operation is carefully conducted, we obtain the pharmaceutical called *koumiss*. A recipe for this liquor was included in N.F. V under the name of "*lac fermentatum.*"

The original koumiss was made in Russia by fermenting mares' milk with a peculiar ferment, *kephir.*

Condensed milk is milk evaporated in vacuo, and usually preserved by addition of cane sugar.

Solid evaporated milk is now on the market; one brand—"Nutrium"—consists of 40 per cent proteids, 45.7 per cent sugar of milk, 8.57 per cent lime salts and other minerals, and 5.73 per cent of moisture. These powders are made by spraying the milk into a heated revolving cylindrical dryer. It is said that 100 pounds skim milk give 10 pounds nutrium.

Infant's foods, of which there are a great host, can be grouped into the following classes:

Milk Foods.—Such as condensed milk. Bad as exclusive infant diet.

Predigested Foods.—Milk foods digested with pepsin or pancreatin.

Cereal Foods.—Grains dextrinized by heat. To be used mixed with milk.

Malted Foods.—Cereals digested with milk and then dried. Used mixed with milk.

Mixed Foods.—(*a*) Combinations of extract of barley or wheat with powdered predigested milk.

(*b*) Dextrinized cereals with unpredigested milk powder.

ANIMAL DRUGS

At this place we will discuss those drugs of animal origin—whole animals, animal organs, and animal excretions—which are of such complex composition that they cannot be classed among definite chemicals. As examples of animal products that are definite chemicals may be cited *lactic acid* (p. 677), the animal *fats*, *oils*, and *waxes* discussed in Chapter XLI, and the animal proteins, *pepsin* and *pancreatin*, discussed on the foregoing pages of this chapter. The discussion of the other animal products in this chapter may be misleading, inasmuch as some of the products here considered are not albuminoidal in character. However, as the characteristic compounds of most living animal tissue are protein matter, it seems appropriate to discuss animal drugs at this place, with the warning given above.

The drugs to be considered may be classified as follows:

Whole animals
- Cantharides, U.S.P.
- Cochineal, U.S.P.

Animal organs
- Egg, N.F.
- Egg yolk, N.F.
- Isinglass, U.S.P. 1890
- Musk, U.S.P. IX
- Thyroid, U.S.P.
- Solution of parathyroid, U.S.P.
- Thyroxin, U.S.P.
- Total pituitary, N.F.

Animal organs
- Anterior pituitary, N.F.
- Posterior pituitary, U.S.P.
- Liver extract, U.S.P.
- Solution of liver, U.S.P.
- Solution of liver, purified, U.S.P.
- Stomach, U.S.P.
- Corpus luteum, N.F.
- Ovary, N.F.
- Ovarian residue, N.F.

Animal excretions
- Oxgall, U.S.P.
- Milk, N.F.

CANTHARIS—Cantharides

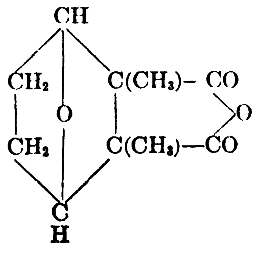
(**Canthar.**—Spanish Flies, Russian Flies, Pulvis Cantharidis P.I.)

Cantharides consists of the dried insects, *Cantharis vesicatoria* (Linné) De Geer (Fam. *Meloideæ*).

Cantharides yields not less than 0.6 per cent of cantharidin and not more than 10 per cent of moisture, U.S.P., p. 473.

Storage.—Preserve in tightly-closed containers.

Constituents.—*Cantharidin*, $C_{10}H_{12}O_4$, wax, fat, etc. Cantharidin, the vesicating principle, is the anhydride of cantharidinic acid. Gadamer thinks that its graphic formula is



It is a neutral principle and might therefore be discussed more properly in Chapter XLVIII.

Remarks.—Cantharides are beetles, which differ from flies in having cases into which they fold their wings. The active principle is cantharidin, which produces the irritating effects of the drug, and which is sublimable. Hence care must be observed in hovering over melting cantharides cerate, as thereby severe irritation of the eyes may ensue.

Medical Properties.—Aphrodisiac, vesicant, stimulant to scalp. Administered internally (rarely nowadays) in the form of the official *tincture* (p. 245). Externally as the official *cerate* (p. 361), properly spread as the official *plaster* (p. 377).

COCCUS—Cochineal

Cochineal consists of the dried female insects *Coccus cacti* Linné (Fam. *Coccidæ*), enclosing the young larvæ.

Constituents.—*Carminic acid* (p. 882), wax, and fat; not more than 6 per cent ash.

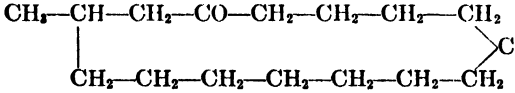
Remarks.—Cochineal is the female insect gathered while with young. Carminic acid, $C_{22}H_{22}O_{13}$, is discussed among the coloring principles on page 882. *Carmine* is the insoluble form of carminic acid, made by precipitating an infusion of cochineal with either alum or potassium bitartrate.

Medical Properties.—Used entirely as a color. For this purpose, however, *solution of carmine,* N.F. (p. 213) and *cochineal color,* N.F. (p. 213) are usually employed.

Ovi Vitellum Recens (U.S.P. 1890; N.F. VI), or *Yolk of Egg,* contains 50 per cent of fixed oil emulsionized by proteins (vitellin, livitin, etc.). The yolk contains about 12 per cent of lecithin (p. 746) and a yellow coloring matter called "ovochromin." It is used as a protective dressing and for making emulsion of cod liver oil (p. 288).

Ichthyocolla (U.S.P. 1890), or *Isinglass,* represents the dried "sounds" (swimming bladders) of the Russian sturgeon, *Acipenser huso,* whose eggs (roe) constitute that delicacy, caviar. It is almost pure gelatin, and is the adhesive constituent of court plaster. (*Emplastrum Ichthyocollæ,* U.S.P., 1890.)

Moschus (U.S.P. IX) or *Musk,* is the contents of little sac situated between the navel and the penis of the musk deer (*Moschus Moschiferus*), a small animal living in the mountains of Central Asia. Musk contains ammonia, cholesterin, fat, wax, odorous principle, *muskone,* etc. It is used largely in perfumery and it must be borne in mind that synthetic musk (p. 836) has nothing in common with the drug except similarity in odor. Musk is used as a powerful stimulant in 4-grain doses.



Ambergris is a morbid secretion of the liver or intestines of the spermaceti whale. Lumps of ambergris are found occasionally along the seashore and command high prices because of its value in perfumery. The gray or brown pieces have a characteristic odor which causes them to be in demand as a fixative (p. 836).

THE ENDOCRINES

These are the ductless glands, whose secretions are passed directly into the blood. The active principles of these endocrines are called *hormones.* Among the endocrines we find such glands as the *thyroid,* the *suprarenal,* the *pituitary,* and others described below. Figure 272 shows the location of these glands in the animal body.

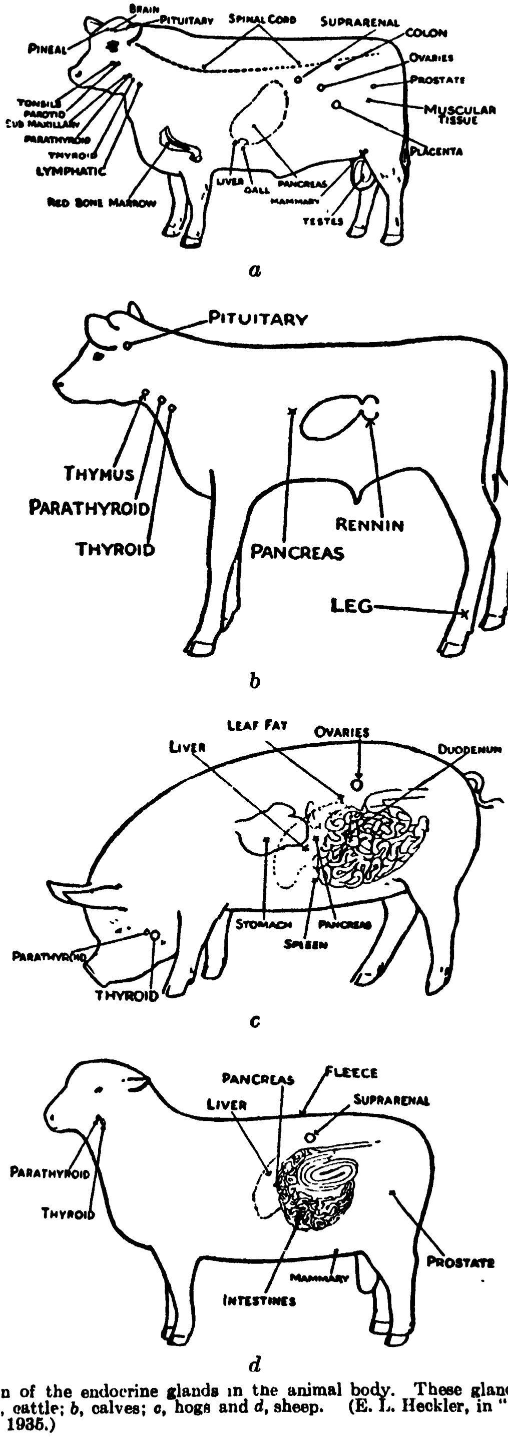


Fig. 272.—Location of the endocrine glands in the animal body. These glands are the sources of medicinal products: *a*, cattle; *b*, calves; *c*, hogs and *d*, sheep. (E. L. Heckler, in "American Professional Pharmacist," August, 1935.)

The table on p. 963 constitutes a useful summary of the endocrine glands.

THYROIDEUM—Thyroid

(Thyroid.)

Thyroid is the cleaned, dried and powdered thyroid gland previously deprived of connective tissue and fat. It is obtained from domesticated animals that are used for food by man.

Storage.—Preserve in an air-tight container, in a cool place.

Summarized Description.

Yellowish, amorphous powder; characteristic odor; saline taste. For details, see U.S.P., p. 388.

For *tests for identity* and for *assay*, see U.S.P., p. 388.

Constituents.—*Thyroxin* (see below); combined with proteid matter, etc.

Remarks.—The thyroid gland is found in the neck of man and other animals and its abnormal development represents the disease called goiter. The activity of the gland, when used as medicine, is proportional to its organic iodine content; some specimens containing ¼ of 1 per cent.

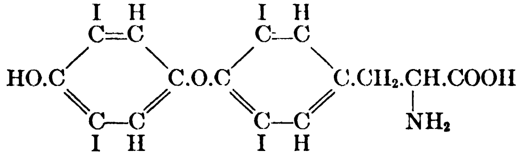
Medical Properties.—Furnishes iodine in nonirritating and easily absorbable form. Used in goiter, obesity, etc.

Dose.—60 mg. (1 grain).

THYROXINUM—Thyroxin

(Thyrox.)

$C_{15}H_{11}O_4NI_4$



Molecular weight, 776.77

Thyroxin is an active physiological principle obtained from the thyroid gland, or prepared synthetically, and contains not less than 64 per cent of iodine as an integral part of the Thyroxin molecule.

Summarized Description.

White acicular crystals or powder; insoluble in water and practically insoluble in alcohol and other organic solvents; soluble in alcohol containing mineral acids and in solutions of alkaline hydroxides. For details, see U.S.P., p. 389.

For *tests for identity* and for *impurity* (soluble iodide), see U.S.P., p. 389.

For *assay*, see U.S.P., p. 389.

Remarks.—This substance was isolated by Kendall from the thyroid gland. There has been some controversy as to the structure of this hormone, but the formula proposed by Harrington (given above) is generally accepted. This substance has been prepared synthetically.

Medical Properties.—Thyroxin is used similarly to dried thyroids only in smaller doses.

Dose.—½ mg. (1/120 grain).

LIQUOR PARATHYROIDEI—Solution of Parathyroid

(Liq. Parathyroid.—Parathyroid Extract)

Solution of Parathyroid contains the water-soluble principle or principles of the parathyroid glands which have the property of relieving the symptoms of parathyroid tetany and of increasing the calcium content of the blood serum in man and other animals. It is obtained from the fresh parathyroid glands of healthy domesticated animals used for food by man. The parathyroid glands must be removed from the animals immediately after slaughtering, and then extracted at once or kept frozen until extracted. The glands are freed from gross fat and connective tissue, ground, extracted,

THE ENDOCRINE GLANDS

(Compiled from data kindly furnished by Reed and Carnrick)

Gland.	Function.	Symptoms of		Therapeutic indications.
		Hypersecretion.	Hyposecretion.	
Ovaries. Testes.	Reproduction; and influences metabolism and mental activity.	Early maturity; precocious sex development.	In female: obesity; neurasthenia; amenorrhea; dysmenorrhea. In male functional impotency; climacteric.	All states of insufficiency of the female sex glands. All types of hypofunction of the male sex glands.
Prostate. (Internal secretion doubtful)	Maintenance of motility and viability of spermatozoa		Functional impotency.	Sterility; prostatitis; prostatic hypertrophy; neurasthenia.
Thyroid.	Stimulates metabolism and energy production, controls iodine metabolism.	High basal metabolism, tachycardia, tremor, loss of weight; nervous irritability, moist skin, long slender bones; toxic goiter	Low basal metabolism; slow pulse, low blood pressure; mental and physical sluggishness; obesity, dry skin and hair; short stubby bones	Cretinism and myxedema; hypothyroidism; menstrual disorders, obesity; senility; general adynamia.
Parathyroid.	Regulation of calcium metabolism.	Extreme hypercalcemia.	Tetany, eclampsia, paralysis agitans, epilepsy; spasmophilia; muscular dystrophies	Convulsions; tetany; Thomsen's disease, diarrhea; prolonged menstrual bleeding, hypocalcemia
Thymus. (Internal secretion doubtful)	Source of lymphocytes, and leukocytes, influences growth of young			Arthritis deformans; rickets.
Pituitary. **Posterior Lobe.**	Stimulates plain muscle; regulates carbohydratemetabolism, regulates water balance.	Not identified as an uncomplicated clinical entity.	Dystrophia adiposo-genitalis, increased carbohydrate tolerance.	Delayed labor; asthma; diabetes insipidus; retention of urine; menorrhagia; shock; deficient general and sexual development; obesity.
Anterior Lobe.	Regulates somatic growth and normal development of gonads	Gigantism in adolescence, acromegaly in adults	Lorain type of infantilism.	Physical infantilism.
Pineal.	Influences somatic and gonadal growth.	Accelerated development of gonads, mental precocity, increased growth of skeleton (in the young)	Mental retardation.	Retardation; over- and underdevelopment of sex glands; muscular dystrophies
Adrenals.	**Cortex**—imperfectly understood **Medulla**—production of epinephrine	Virilism, in males clinically negative.	No clinical symptom-complexes, except perhaps pigmentation in Addison's disease, asthenia	Asthenia, Addison's disease; cardiac weakness, hypo- and hypertension.
Spleen.	Formation of a hormone which regulates the hematopoietic tissues	Leukemia.	Anemia; malaria; vasomotor disturbances	
Pancreas, Isles of Langerhans.	Controls carbohydrate metabolism		Hyperglycemia; glycosuria; ketonuria	Diabetes mellitus; obesity; malnutrition; intestinal indigestion.
Liver.	Production of urea and glycogen.			Hepatitis; congestion; cirrhosis; diminished hemoglobin and red blood cell count.
Mammary. (Int. sec. in disp.)	Secretion of milk; galactagogue, involution of uterus.	Breast hyperplasia, abnormal breast growth.	Arrest of breast activity	Menorrhagia of menopause; profuse menstruation; scanty secretion of milk.
Kidney. (Internal secretion in dispute.)	Secretion of urine; controls protein metabolism.			Acute and chronic nephritic conditions; prophylactic in kidney complications; eclampsia and albuminuria in pregnancy.

and purified to make it suitable for parenteral administration. The solution is then adjusted to the proper potency by assay.

One cc. of Solution of Parathyroid possesses a potency equivalent to not less than 80 parathyroid units and not more than 120 parathyroid units, each unit representing one-hundredth of the amount required to raise the calcium level of 100 cc. of the blood serum of normal dogs 0.001 Gm., within from sixteen to eighteen hours after administration. The solution must be sterile.

Storage.—Preserve in air-tight containers, preferably in a cool place.

Summarized Description.

None given in U.S.P. XI.

For *assay*, see U.S.P., p. 217.

Remarks.—The rubric given above gives a comprehensive explanation of the preparation of the solution from the parathyroid glands. It is administered by subcutaneous injection for the purpose of maintaining or raising the calcium content of the serum. According to competent medical authorities, its oral administration is of little value.

The Pharmacopœia provides an appropriate assay expressed in "parathyroid units."

Dose.—By hypodermic injection, 25 units.

PITUITARIUM POSTERIUS—Posterior Pituitary

(Pituitar. Post.—Pituitarium U.S.P. X, Pituitary, Hypophysis Sicca)

The cleaned, dried, and powdered posterior lobe obtained from the pituitary body of domesticated animals which are used for food by man. The pituitary body must be removed from the animal immediately after slaughtering and then dried at once or kept frozen until dried.

Storage.—Preserve in well-closed containers, in a cool place.

Summarized Description.

Yellowish or grayish amorphous powder; characteristic odor; partially soluble in water. For details, see U.S.P., p. 292.

Remarks.—This official substance is the posterior lobe of the pituitary gland, which is a pale reddish body attached to the under surface of the cerebrum. This gland not only exercises a marked influence on the brain wherein it is found but also on the entire growth of the animal. The posterior lobe contains a substance having distinct action upon the muscles of the blood vessels and the uterus. A biological assay is provided under *Liquor Pituitarii Posterioris* (see below).

Medical Properties.—Used in various forms of hemorrhage.

Dose (U.S.P. X).—30 mg. (½ grain).

LIQUOR PITUITARII POSTERIORIS—Solution of Posterior Pituitary

(Liq. Pituitar. Post.—Liquor Pituitarii U.S.P. X, Solution of Pituitary)

Solution of Posterior Pituitary contains the water-soluble principle or principles from the fresh posterior lobe of the pituitary body of healthy domesticated animals used for food by man. The pituitary body must have been removed from the animal immediately after slaughtering, and then extracted at once or kept frozen until extracted. One cc. of Solution of Posterior Pituitary produces an activity upon the isolated uterus of the virgin guinea-pig, corresponding to not less than 80 per cent and not more than 120 per cent of that produced by 0.005 Gm. of the standard powdered posterior pituitary, prepared as herein directed. The solution must be sterile.

Storage.—Preserve in small, well-filled, amber-colored containers or in ampuls.

Summarized Description.

Almost colorless transparent liquid; faint characteristic odor. For details, see U.S.P., p. 217.

For *assay*, see U.S.P., p. 217.

Remarks.—The above description of this official solution, when read with what has just been said about the pituitary gland, is self-explanatory.

Dose.—By hypodermic injection, 1 cc. (15 minims).

Pituitarium Totum (N.F. VI), or *Whole Pituitary*, is the dried, partially defatted and powdered pituitary gland of cattle, sheep or swine. This represents the entire gland. The posterior lobe is recognized by U.S.P. XI (see above) while the anterior lobe is described in the Formulary (see below). Obviously the total pituitary combines the medicinal action of both the posterior and anterior lobes. *Dose.*—60 mg. (1 grain).

Pituitarium Anterior (N.F. VI) is the dried partially defatted and powdered anterior lobe of the pituitary gland of cattle, sheep or swine. Both this and the whole pituitary (see above) are standardized in the Formulary, by a histological description.

From the *anterior* lobe of the pituitary body, Robertson has isolated the growth-controlling principle, which he named *tethelin.* Its chemical composition is not yet known but it hydrolyzes to unsaturated fatty acid soaps and inosite and contains an imine-azoyl group.

Dose.—0.3 Gm. (5 grains).

Pituitary Hormones.—Kamm and others report that the *anterior* pituitary contains two hormones; one affecting bodily growth; the other influencing the development of the sex organs. From the *posterior* pituitary, Kamm has isolated two hormones; one a pressor; the other an oxytocic principle. These two hormones are now marketed under the names, *pitressin* (or beta-hypophamine) and *pitocin* (or alpha-hypophamine) respectively.

Suprarenalum (N.F. VI), or *Dried Adrenal Substance*, is the partially defatted and powdered suprarenal gland of cattle, sheep or hogs. This is a gland situated above the kidney, as the name suggests. It contains epinephrine (p. 817), fat, proteids, ash, etc. This gland increases blood pressure and is therefore of value in shock. It relieves inflammation of the mucous membrane and is therefore recommended for catarrh and hay fever. *Dose.*—250 mg. (4 grains).

Cortin is a hormone isolated by Hartman from cortex of the suprarenal gland. It is at the present time so rare that it is not commercially available. It has been found of marked value in the treatment of Addison's disease.

EXTRACTUM HEPATIS—Extract of Liver

(Ext. Hepat.—Dry Liver Extract)

Extract of Liver contains that soluble fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons suffering from pernicious anemia. This fraction, which has been dried, conforms to the specifications outlined under *Standardization of Products for the Treatment of Pernicious Anemia* (see U.S.P., p. 484).

Storage.—Preserve in well-closed containers, and preferably in a cool place.

The official monograph on liver extract provides no "Summarized Description." It directs the standardization of the product as per rules laid down by the "U.S.P. Anti-anemic Preparations Advisory Board" (see U.S.P., p. 484).

Remarks.—In 1927, Minot and Murphy reported the successful treatment of pernicious anemia by means of diets containing large amounts of liver. While such diets were extremely effective, they become distasteful to the anemia patient. Cohn and others have prepared liver concentrates which are now largely employed. The purpose of the new official monograph is to provide standards for such preparations.

There has, of course, been research as to the reason why liver is so useful in anemia. Dakin and others believe that liver contains a compound of beta-hydroxyglutamic acid and hydroxyproline and that this is the factor which relieves anemia. Other investigators ascribe the value of liver to the iron and copper that it contains (p. 557).

Dose.—To be stated on the label of the container.

LIQUOR HEPATIS—Solution of Liver

(Liq. Hepat.—Liquid Extract of Liver)

Solution of Liver contains that soluble fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons suffering from pernicious anemia, and conforms to the specifications outlined under *Standardization of Products for the Treatment of Pernicious Anemia* (see U.S.P., p. 484).

Storage.—Preserve in well-closed containers, and preferably in a cool place.

Summarized Description.

Not given in U.S.P. XI.

Assay.—See "Remarks" under *Extractum Hepatis.*

LIQUOR HEPATIS PURIFICATUS—Purified Solution of Liver (Liq. Hepat. Purif.—Parenteral Solution of Liver)

Purified Solution of Liver contains that soluble fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons suffering from pernicious anemia, and is prepared for parenteral use. When given by parenteral injection to patients suffering from pernicious anemia in relapse, it conforms to the specifications outlined under *Standardization of Products for the Treatment of Pernicious Anemia* (see U.S.P., p. 484).

The solution must be sterile and may not contain more than 0.5 per cent of cresol or of phenol.

Storage.—Preserve in well-closed containers and in a cool place.

Summarized Description.

Not given in U.S.P. XI.

Assay.—See "Remarks" under *Extractum Hepatis.*

Remarks.—These liquid forms of liver preparations are designed to cover the reliable brands of this now popular medicament.

Dose.—To be stated on the label of the container.

FEL BOVIS—Ox Bile

(Oxgall)

Ox Bile is the fresh bile of the ox, *Bos taurus* Linné (Fam. *Bovidæ*).

Summarized Description.

Brown-green or dark green viscid liquid; disagreeable bitter taste. For details, see U.S.P., p. 161.

For *tests for identity,* see U.S.P., p. 161.

Constituents.—Sodium salts of *glycocholic acid* and *taurocholic acid; lecithin; cholesterin* (p. 747); the bile pigments, bilirubin (p. 882), biliverdin, etc.; mucin; water, 85 per cent. The two acids above mentioned are combinations of *cholic* (or *cholaic*) *acid,* $C_{21}H_{40}O_5$, with glycocoll (p. 671), and with taurin (p. 671) respectively.

Remarks.—Bile is the secretion of the liver, and is designed to emulsionize and assimilate fats. The official test, depending on the play of colors, when bile is treated with sugar and sulfuric acid (Pettenkofer's test), is very characteristic.

Medical Properties.—Laxative and cholagogue. Almost invariably used in the official *extract* (p. 300).

STOMACHUS—Stomach

(Stomach.—Dried Stomach)

Stomach is the dried and powdered defatted wall of the stomach of the hog, *Sus scrofa* var. *domesticus* Gray (Fam. *Suidæ*). It contains that antianemia factor which causes an increase in the number of red blood corpuscles in the blood of persons suffering from pernicious anemia. This substance conforms to the specifications outlined under *Standardization of Products for the Treatment of Pernicious Anemia* (see U.S.P., p. 484).

Storage.—Preserve in well-closed containers, preferably in a cool place.

Summarized Description and *Assay,* see *Extractum Hepatis* (p. 965).

Remarks.—As stated above, this new official is used as an adjunct in the modern treatment of pernicious anemia.

Dose.—To be stated on the label of the container.

Corpus Luteum (N.F. VI) is the dried undefatted and powdered corpus luteum obtained from the ovary of cattle, sheep or swine. One commercial form is called *lutein.* It is used in menorrhagia and in readjustment of the endocrines at the menopause. It is interesting to note that the Formulary standardizes quality by microscopic appearance. *Dose.*—300 mg. (5 grains).

Ovarii (N.F. VI) is the dried undefatted and powdered ovary of cattle, sheep and swine. It is a brown powder of characteristic odor and is evaluated by the histological description given in the Formulary. Ovary is used in menstrual disturbances and in surgical and natural menopause. *Dose.*—0.3 Gm. (5 grains).

Residuum Ovarium (N.F. VI), or *Ovarian Residue,* represents the dried undefatted and powdered ovary deprived of its corpus luteum. It is used in medicine for the same purposes as the entire ovary. *Dose.*—0.3 Gm. (5 grains).

Pancreas is the abdominal salivary gland, secreting the pancreatic juice (from which pancreatin is obtained) and furnishing from the interalveolar cell areas a principle capable of reducing the quantity of blood sugar and the excretion of sugar from the urine of diabetics. The principle is called *insulin.*

Insulin was isolated by Banting and Best in 1922. From the original product, Abel and others have secured insulin in crystalline form. To these crystals have been ascribed the following formulæ:

Funk	*Abel*
$C_{69}H_{102}O_{22}N_{18}S$	$C_{45}H_{69}O_{14}N_{11}S$

Since Svedberg's investigations indicate that insulin has the molecular weight of about 35,100, its gross structure must be much greater than the percentage formulæ given above.

Commercial insulin is prepared from the pancreatic gland material by the following stages: (*a*) extraction with acidulated alcohol, (*b*) concentration of the alcoholic extract, (*c*) precipitation of insulin by addition of ammonium sulfate, (*d*) purification of the precipitated insulin by the Dudley picrate method, (*e*) standardization and preparation of the final product. As already stated, insulin is an extremely valuable agent in the treatment of diabetes. Carr states that 0.00005 Gm. of the purest available insulin (1926) will cause the disappearance of 3 Gm. of sugar from the blood within two hours.

Like all eminently successful medicaments, the introduction of insulin has brought into commerce several products offered as less expensive substitutes. Among these may be cited *synthalin* (or decamethylene diguanidine) and *myrtillin,* an extract of the leaves of the blueberry plant.

Sex Hormones.—From the ovarian follicles and from the urine of pregnant women, two hormones have been isolated. One is called *ketohydroxyœstrin,* $C_{18}H_{22}O_2$ and the other is *trihydroxyœstrin,* $C_{18}H_{24}O_3$. The first is known commercially as *Theelin* or *Progynon,* the other is called *Theelol.* Both are used in the treatment of female sexual insufficiency.

Grant (1935) and also Addinall (1935) have illustrated by graphic formulæ the remarkable similarity in the structure of certain sexual hormones with certain vitamins and certain plant principles having medicinal value.

BIBLIOGRAPHY

Proteins.—(General) Kossel, B., 34, 1901, 3215; Fischer, Ph. Jl., 78, 1907, 260. (History) Levene, Science, 74, 1931, 658. (Nomenclature) Beguin, Schw. Apoth. Zt., 66, 1928, 193. (Classification) Joint Committee, Proc. Ch. Soc., 23, 1907, 55. (Syntheses) Fischer, B., 40, 1907, 3544; Plimmer, Jl. Ch. Soc., 99, 1911, 1386. (Composition) Johns and Jones, C.A., 13, 1919, 847; Kolthoff, C.A., 20, 1926, 58; Harris, C.A., 25, 1931, 15; Abderhalden and Reich, C.A., 25, 1931, 526; Rimington, C.A., 25., 1931, 3677; Lloyd and Phillips, Jl. Soc. Ch. Ind., 51, 1932, 163. (Molecular weight) van der Feen, C.A., 10, 1916, 1986; Cohn and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 564B; Svedberg and co-workers, Jl. Am. Ch. Soc., 48, 1926, 3081; *ibid.*, 51, 1929, 2170; *ibid.*, 52, 1931, 279, 3282, 3650 and 4400; C.A., 26, 1932, 1948 and 3165; Nichols, Jl. Am. Ch. Soc., 52, 1930, 5176; Astbury and Woods, C.A., 25, 1931, 3366.

Proteoses.—Osborne, Jl. Am. Ch. Soc., 19, 1897, 525.

Serum Albumin.—Osborne, Jl. Am. Ch. Soc., 21, 1899, 477.

Nucleinic Acid.—Javillier, Dr. Circ., 69, 1925, 347.

Egg-albumin.—White, Ph. J., [3], 23, 1892, 450; Hopkins, Jl. Physiology, 23, 1898, 131 and 25, 1900, 306; Osborne, Jones and Leavenworth, Am. Jl. Physiol., 24, 1909, 252; Pictet and Cramer, Jl. ph. ch., 20, 1919, 282; Calvery, C.A., 26, 1932, 2204.

Solution of Ferric Albuminate.—Lillig, Ap. Zt., 26, 1911, 589, 597, 605, 620, 638, 648 and 659; Bechhold, C.A., 23, 1929, 167.

Solution of Peptones with Manganese.—Dunning, A.Ph.A., 53, 1905, 397; Harrison, A.J.P., 80, 1908, 162.

Peptone.—Kühne and Crittenden, Zt. Biol., 22, 1886, 423; Heaton and Vasey, A.J.P., 64, 1892, 154; Gerrard, Ph. Jl., 56, 1896, 276; Scoville and Howard, Dr. Circ., 42, 1898, 287; Eccles, A.Ph.A., 34, 1886, 83; Maly, *ibid.*, 29, 1881, 365; Chapoteaut, *ibid.*, 29, 1881, 366; Pettit, *ibid.*, 30, 1882, 457; Darby, *ibid.*, 27, 1879, 543; Herth, *ibid.*, 28, 1880, 362.

Syntonin.—Bilteryst, Ch. Cent., 722, 1901, 502.

Casein.—(Manufacture) Chappell, C.A., 25, 1931, 1917. (Composition) Lindet, C.A., 6, 1912, 3099. (Molecular weight) Svedberg and co-workers, Jl. Am. Ch. Soc., 52, 1930, 241 and 701; Carpenter, *ibid.*, 53, 1931, 1812.

Gelatin.—(History) Leffmann, Jl. Frank. Inst., 194, 1922, 564. (Composition) Skraup and Biehler, C.A., 4, 1910, 441; Abderhalden and Schmitz, C.A., 24, 1930, 5761. (Manufacture) Anon., Am. Dr., 18, 1889, 214; Thiele, Ch. Zt., 36, 1912, 418 and 451; Bogue, Jl. Ind. Eng. Ch., 14, 1922, 795. (Uses) Beal and Neff, Jl. A.Ph.A., 17, 1928, 261; Smith, Ph. Jl., 122, 1929, 617. (Gelatinization) Procter, Jl. Ch. Soc., 100, 1911, 342; Von Veimarn, C.A., 5, 1911, 2771; Washburn, C.A., 8, 1914, 2760; De Jong, C.A., 17, 1923, 2527.

Gelatin Solution.—Forrester, Am. Dr., 55, 1909, 209.

Keratin.—Zuntz, Ph. Jl., 105, 1920, 323; Speakman and Hirst, C.A., 26, 1932, 1449; Rimington, C.A., 26, 1932, 3381.

Hemoglobin.—Schunck and Marchlewski, B., 29, 1896, 2877; Piloty and Fink, B., 45, 1912, 2495; Barcroft, Jl. Soc. Ch. Ind., 45, 1926, 126 and 47, 1928, 609; Ferry and Green, C.A., 18, 1924, 2536 and 23, 1929, 1915; Fischer, B., 60B, 1927, 2611 and Zt. angew. Ch., 44, 1931, 617.

Hematin.—(Composition) Piloty, A., 377, 1910, 314; Willstatter, Jl. Am. Ch. Soc., 37, 1915, 323. (Preparation) Sollmann, A.J.P., 74, 1902, 275. (Use) Brown, Jl. Exp. Med., 15, 1912, 579.

Enzymes.—Czapek, Biochemie der Pflanzen, 1913; Tschirch, Pharm. Era, 46, 1913, 595; Arny, Dr. Circ., 59, 1915, 240; Dunbar, Ph. Zt., 48, 1903, 226; Lowdermilk, Jl., A.M.A., 63, 1914, 141; Tschirch, Pharm. Era, 47, 1914, 54; Berg, C.A., 8, 1914, 2891; Maryott, Jl. A.Ph.A., 4, 1915, 678; Prescott, A.J.P., 87, 1915, 63; Borkorny, C.A., 1915, 2907 and 14, 1920, 2497; Herzog, C.A., 15, 1921, 691; Sieburg and Mordhorst, C.A., 14, 1920, 2497; von Euler, B., 55, 1922, 3583; Willstatter, B., 55, 1922, 3601 and 55B, 1922, 509; Dernby, Jl. Soc. Ch. Ind., 42, 1923, 322A; Sadtler, A.J.P., 95, 1923, 275; Rosenthaler, Ph. Cent., 66, 1925, 305; Fischer and Hilmer, C.A., 19, 1925, 2347; Bansi and Ucko, C.A., 21, 1927, 105 and 3911; Leffmann, Jl. Frank. Inst., 207, 1929, 286; Dryerre, Nat. Dr., 58, 1929, 287; Ed., Jl. Soc. Ch. Ind., 49, 1930, 23; Waldschmidt-Leitz, C.A., 25, 1931, 5440; Anon., Jl. Soc. Ch. Ind., 50, 1931, 690; Fernández and Pizarrosa, C.A., 26, 1931, 4290; Eggleton, Science Prog., 25, 1931, 393; von Euler, C.A., 25, 1931, 5183; Mueller, Ph. Zt., 77, 1932, 381, 404 and 416; Jackson, Ph. Jl., 129, 1932, 397; Anon., A.J.P., 105, 1933, 12; Falk, Science, 81, 1935, 471.

Amygdalase.—Schar and Rosenthaler, Ch. Zt., 35, 1911, 908.

Diastase.—(General) Takamini, A.J.P., 70, 1898, 137. (Manufacture) Payen, Am. Dr., 16, 1887, 232; Lyalin, C.A., 5, 1911, 3833. (Composition) Buraczewski, C.A., 6, 1912, 1757; Ehrich, C.A., 18, 1924, 3387; Willstätter and Kumagawa, Jl. Soc. Ch. Ind., 44, 1925, 777B; Nishimura, *ibid.*, 45, 1926, 104B. (Properties) Baker and Hulton, Jl. Ch. Soc., 105, 1914, 1529.

Emulsin.—Bertrand and Compton, C.A., 6, 1912, 1756; Helferich and co-workers, C.A., 24, 1930, 4309; C.A., 25, 1931, 4014; C.A., 26, 1932, 3286 and 4070.

Linase.—Armstrong and Eyre, C.A., 7, 1913, 1203.

Lipases.—Tantzov, C.A., 8, 1914, 2629.

Pancreatin.—(Composition) Eberhardt, Am. Dr., 18, 1889, 190; Vernon, A.Ph.A., 50, 1902, 1082; Le Breton, C.A., 26, 1932, 3811; Northrup and Kunitz, Science, 73, 1931, 262. (Manufacture) Anon., A.J.P., 49, 1877, 351. (Therapeutic action) Toplis, Proc. Pa. Ph. A., 42, 1919, 273.

Papain.—Watts, A.Ph.A., 50, 1902, 1076; Mansfield, Jl. A.Ph.A., 3, 1914, 169; Anon., Ch. and Dr., 93, 1920, 1663; Sanyal, C.A., 16, 1922, 3731; Willimott, Ph. Jl., 121, 1928, 219; Sen, C.A., 25, 1931, 4355.

Pepsin.—(History) Squire, Ph. Jl., 16, 1857, 474; Fairchild, A.J.P., 74, 1902, 53 and 105. (Composition) Fairchild, see above; Sacks, A.Ph.A., 57, 1909, 1122; Elbonger and Funk, Nat. Dr., 58, 1929, 116; Becker, N.F. Comm. Bull., Feb. 17, 1933, 710. (Crystalline) Northrup, Science, 69, 1929, 580; Levene, *ibid.*, 73, 1931, 494. (Manufacture) Marshall, A.Ph.A., 51, 1903, 980; Webber, A.Ph.A., 40, 1892, 1072. (Incompatibilities) Sollmann, A.Ph.A., 55, 1907, 948; Tocher, A.Ph.A., 55, 1907, 950; Petit, Jl. de ph. et ch., [7], 1, 1910, 150. (Activity) Apple, Proc. A.Ph.A., 58, 1910, 1125; Graber, Jl. A.Ph.A., 10, 1921, 437; Fenger, Jl. Am. Ch. Soc., 45, 1923, 249; Anon., Jl.

A.Ph.A., 18, 1929, 165; Schenk, Apoth. Zt., 47, 1932, 987. (Testing) Traut and Vahlteich, Jl. A.Ph.A., 11, 1922, 686.

Prunase.—Armstrong and Horton, C.A., 7, 1913, 1202.

Rennin.—Fenger, Jl. Am. Ch. Soc., 45, 1923, 249; Balls, Sigma Xi Quart., 19, 1931, 103.

Urease.—Van Slyke and Cullen, Jl. A.M.A., 62, 1914, 1558; Wester, also Yumazaki, Yearbook, A.Ph.A., 9, 1920, 665 and 666; Dox, A.J.P., 92, 1920, 153; Mack and Villars, Jl. Am. Ch. Soc., 45, 1923, 501 and 505; Sumner, Science Supp., 64, No. 1663, 1926, X; Waldschmidt-Leitz and Steigerwaldt, C.A., 25, 1931, 2446.

Zymase.—Lebedev, also Rinckleben, C.A., 5, 1911, 3839 and 6, 1912, 269 and 1807.

Toxins.—White, Ph. Jl., 94, 1915, 156; Couch, A.J.P., 96, 1924, 747.

Abrin.—Durham, C.A., 8, 1914, 2002.

Ricin.—Durham, see above; Spaeth and Tschlenitz, C.A., 16, 1922, 1070; Dowzard, Jl. A.Ph.A., 12, 1923, 116; Fodera, C.A., 24, 1930, 891.

Crotin.—Karrer and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 650B.

Pollen Toxins.—Heyl, Jl. Am. Ch. Soc., 39, 1917, 1470 and 42, 1920, 1738; Paton, C.A., 15, 1921, 1742; Walker, 15, 1921, 1755; Piness and co-workers, C.A., 18, 1924, 3617; Moore and co-workers, Jl. Am. Ch. Soc., 52, 1930, 3591; *ibid.*, 53, 1931, 2746; C.A., 25, 1931, 1896; Bouillenne, C.A., 25, 1931, 2461; Stull and co-workers, C.A., 25, 1931, 5712; Johnson and Rappaport, C.A., 26, 1932, 2775.

Sting Toxins.—Fleury, Jl. ph. ch., 22, 1920, 438; Anon., Dr. Circ., 73, 1929, 516.

Toad Venom.—Wieland and co-workers, C.A., 26, 1932, 140.

Snake Venom.—Peacock, Jl. A.Ph.A., 17, 1928, 750.

Vitamins.—(General) Eykman (1897), through Vedder, Jl. A.M.A., 67, 1921, 1494; Hopkins, Analyst, 31, 1906, 395; Jl. Physiol., 44, 1912, 425; and Lancet, 91, II, 1913, 1309; Funk, Lancet, 89, II, 1911, 1266; Jl. Physiol., 45, 1913, 489 and 46, 1913, 173; MacCallom and Davis, Jl. Biol. Ch., 15, 1913, 167 and 19, 1914, 245; Stiles, A.J.P., 86, 1914, 237; Seidell, A.J.P., 88, 1916, 410; Jl. Am. Ch. Soc., 44, 1922, 2042; and Jl. Ind. Eng. Ch., 13, 1921, 72; White, Ph. Jl., 97, 1916, 4; Williams, Ph. Jl., 97, 1916, 545; Ramsden, A.J.P., 90, 1918, 507; Owen, A.J.P., 92, 1920, 467; Osborne and Mendel, Ph. Jl., 103, 1919, 186 and C.A., 14, 1920, 3101; Voegtlin and Myers, A.J.P., 91, 1919, 693 and C.A., 14, 1920, 3451; Hess, C.A., 14, 1920, 3266; Hawley, Bull. Pharm., 34, 1920, 448; Haussler, Sch. Ap. Zt., 58, 1920, 621 and 634; Tschirch, Ph. Zent., 61, 1920, 426; Drummond, Jl. Soc. Ch. Ind., 39, 1920, 798A and Ch. News, 123, 1921, 259; Emmett, C.A., 14, 1920, 3097 and Jl. A.Ph.A., 10, 1921, 176; Williams, Jl. Ind. Eng. Ch., 13, 1921, 1107; Harden, Ch. and Dr., 94, 1921, 202; Sherman, C.A., 16, 1922, 735; Heaton, C.A., 17, 1923, 1046; Holmes, Jl. Ind. Eng. Ch., 16, 1924, 295 and 379; Seidell, Science, 60, 1924, 439; Drummond, Jl. Soc. Ch. Ind., 43, 1924, 908; Zilva, *ibid.*, 44, 1925, 445T; Carr, *ibid.*, 45, 1926, 945; Coward, Nat. Dr., 58, 1929, 192; Ed., Jl. Soc. Ch. Ind., 48, 1929, 1083; Schertz, Science, 68, 1928, 50; Pittenger, A.J.P., 100, 1928, 63; McCay, Science, 71, 1930, 315; Wokes, Ph. Jl., 125, 1930, 478; Eddy, Am. Dr., 85, Feb., 1932, 34; Lang, Ph. Jl., 128, 1932, 231; Anon., *ibid.*, 128, 1932, 411; Kazarian, Pract. Dr., 50, July, 1932, 19; Wodlinger and Salmonsen, Jl. Soc. Ch. Ind., 52, 1933, 71; Wood, A.J.P., 105, 1933, 14; Coward, Ph. Jl., 131, 1933, 293. (Vitamin A) Drummond and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 242 and 520; *ibid.*, 48, 1929, 320T and 1071; *ibid.*, 51, 1932, 164; Mayo, Jl. Frank. Inst., 203, 1927, 1; Hess, Science, 57, 1928, 333; Euler, Jl. Soc. Ind., 48, 1929, 1125 and C.A., 26, 1932, 5993; Glanzmann, C.A., 26, 1932, 3013; Van Stolk, Comp. rend., 192, 1931, 1499; Dixon, Jl. Soc. Ch. Ind., 49, 1930, 645 and 663; Ahmad, *ibid.*, 50, 1931, 12T; Morton and Heilbron, C.A., 25, 1931, 133 and 26, 1932, 5993; Karrer, C.A., 26, 1932, 5993. (Vitamin B) Eddy, C.A., 22, 1928, 2193; Williams and Waterman, C.A., 22, 1928, 3907 and Jl. Am. Ch. Soc., 56, 1934, 1187; Randoin and Lecoq, C.A., 22, 1928, 3913; Seidell and Smith, C.A., 25, 1931, 1561; Ohdake, C.A., 26, 1932, 5131. (Vitamin C) Zilva, Jl. Soc. Ch. Ind., 43, 1924, 726B; Szent-Gyorgyi, Biochem. Jl., 22, 1928, 1387; Rygh and co-workers, C.A., 26, 1932, 3005 and 3006; Karrer, A.J.P., 104, 1932, 287; Armstrong, Jl. Soc. Ch. Ind., 51, 1932, 70; Tillmans and Hirsch, C.A., 26, 1932, 5327; Dalmer and Moll, C.A., 26, 1932, 5611; Ott and Packendorff, C.A., 26, 1932, 5611; King and Waugh, Science, 75, 1932, 358; Ehrenstein, Arch. Pharm., 270, 1932, 223. (Vitamin D) Holmes, Jl. Ind. Eng. Ch., 17, 1925, 75; Pract. Dr., 49, March, 1931, 23; Windaus and co-workers, C.A., 22, 1928, 2169, 3666 and 3667; C.A., 26, 1932, 2217; Arch. Pharm., 270, 1932, 191; A.J.P., 105, 1933, 91; Rosenheim and Webster, Jl. Soc. Ch. Ind., 47, 1928, 418; Drummond and co-workers, 44, 1925, 123T; Wokes and Willimott, C.A., 22, 1928, 4585; Genoese and Zallocco, C.A., 22, 1928, 4588; Roussel and Guilhon, C.A., 22, 1928, 4594; Hess and co-workers, Pract. Dr., 47, Nov., 1929, 33 and 48, Nov., 1930, 33; Greenbaum, A.J.P., 101, 1929, 417; Heilbron and co-workers, Nat. Dr., 58, 1929, 155 and Jl. Soc. Ch. Ind., 49, 1930, 180; Bills and co-workers, Pract. Dr., 48, Feb., 1930, 58 and C.A., 24, 1930, 5763; Ed., Ph. Jl., 128, 1932, 241; Anon., *ibid.*, 126, 1931, 79; Remezov, C. A., 26, 1932, 5328; Prather, Nelson and Bliss, Jl.

A.Ph.A., 20, 1931, 1291. (Vitamin E) Evans and co-workers, Pract. Dr., 44, Dec., 1926, 32. (Vitamin G) Seidell and co-workers, Nat. Dr., 58, 1929, 369; Coward, also Reader, Science Supp., 70, Nov. 8, 1929, XIV; Skinner, Merck's Rept., 39, 1930, 151.

Sex Hormones and Vitamin Structure.—Addinall, Merck's Rept., 44, July, 1935, 7; Grant, Canadian Ph. Jl., 69, 1935, 88; Coward, Ph. Jl., 131, 1933, 525; Lundgren, Science, 82, 1935, 130.

Yeast.—(History) Fischer, Schw. Apoth. Ztg., 66, 1928, 343; Frey, Jl. Ind. Eng. Ch., 22, 1930, 1151; Viehoever, A.J.P., 105, 1933, 144; (Biology) Brahmer, C.A., 26, 1932, 5991. (Enzymes of) Neuberg, C.A., 9, 1915, 3075; Borkorny, Yearbook A.Ph.A., 6, 1917, 237; Neuberg, Jl. Soc. Ch. Ind., 44, 1925, 257B. (Other constituents) Jones, A.J.P., 90, 1918, 50; Meisenheimer, Jl. ph. ch., 20, 1919, 361; Stendel and Peiser, C.A., 14, 1920, 2161; MacLean and Thomas, C.A., 14, 1920, 3093; Hinsberg and Roos, C.A., 15, 1921, 2291; Ohdake, C.A., 22, 1928, 1209; Reindel and co-workers, C.A., 22, 1928, 1593 and 24, 1930, 624; Penau and Tanret, C.A., 24, 1930, 2152.

Meat Juices, etc.—Puckner, Jl. A.M.A., 53, 1909, 1754.

Milk Products and Infant Foods.—Remington, A.J.P., 71, 1899, 383; Feil, Proc. O.S.Ph.A., 31, 1909, 56; Stewart, 8th Int. Cong. App. Ch., 18, 1912, 329; England, Proc. Pa. Ph. A., 45, 1920, 245; Wright, Ch. News, 120, 1920, 173; Anon., Ph. Jl., 107, 1921, 449; Wolf, Ph. Zt., 66, 1921, 388.

Cantharides.—(Constituents) Dragendorff, Proc. A.Ph.A., 16, 1868, 257; Foumouze, A.J.P., 40, 1868, 116; Homolka, B., 19, 1886, 1082.

Cantharidin.—Gadamer, Arch. d. Pharm., 252, 1914, 609; 255, 1917, 277 and 290; and 258, 1920, 171; Rudolph, *ibid.*, 254, 1916, 423; Coffey, Jl. Soc. Ch. Ind., 42, 1923, 678A and 1245A; Diels and co-workers, C.A., 23, 1929, 3691; Bruchhausen and Bersch, C.A., 23, 1929, 1647; Stern, C.A., 26, 1932, 5654.

Cochineal.—(History and cultivation) Kraemer, A.J.P., 85, 1913, 344; MacDougall, Ph. Jl., 113, 1924, 689. (Constituents) Pelletiere and Caventou, Jl. de ph., 4, 1818, 193; Dietrich, A.J.P., 40, 1868, 32; Huerre, Jl. de ph. et ch., [7], 4, 1910, 56; Dimroth, B., 42, 1909, 1611 and C.A., 7, 1913, 3479; Becker, C.A., 25, 1931, 6001.

Egg Yolk.—Katz, A.Ph.A., 47, 1809, 583; Plimmer, Jl. Ch. Soc., 93, 1908, 1500; Riedel, C.A., 7, 1913, 802; Serono and Palozzi, C.A., 5, 1911, 2858; Barbieri, C.A., 7, 1913, 92.

Ichthyocolla.—Smith, A.J.P., 3, 1831, 17.

Musk.—(General) Anon., Sch. Wsch. Ch. Ph., 50, 1912, 12; Wagner, C.A., 20, 1926, 3535; Grove-Palmer, Jl. Soc. Ch. Ind., 50, 1931, 845. (History) Anon., Ch. and Dr., 108, 1928, 45. (Sources) Sammons, Pharm. Era, 53, 1920, 74; Charrière, Ch. and Dr., 94, 1921, 451; Bothelo, Pharm. Era, 57, 1923, 47. (Constituents) Blondeau and Guibourt, Jl. de ph., 6, 1820, 105; Anon., A.J.P., 98, 1926, 686; Redgrove, Ch. and Dr., 112, 1930, 288. (Properties) Bazzoni, Yearbook, A.Ph.A., 5, 1916, 234.

Ambergris.—Bruff, C.A., 10, 1916, 1405; Morrison, C.A., 25, 1931, 1696.

Endocrines and Hormones.—Sieg, J. A.Ph.A., 3, 1914, 1138; Anon., Bull. Pharm., 34, 1920, 73, 118, 151 and 205; Anon., Merck's Rept., 33, 1924, 60; 34, 1925, 106; Pittenger, Jl. A.Ph.A., 14, 1925, 99; Carr, Jl. Soc. Ch. Ind., 45, 1926, 241T; Mond, *ibid.*, 45, 1926, 538; Abel, Science, 66, 1927, 337; Bennett, Ph. Jl., 121, 1928, 77; Rapp, Ph. Zt., 76, 1931, 260, 666 and 679; Harrow, Jl. Ch. Ed., 8, 1931, 661.

Thyroid Glands.—Beebe, A.J.P., 83, 1911, 56; Hausler, Schw. Ap. Zt., 53, 1915, 32 and 46; Van Os, Ph. Week., 55, 1918, 1426; Carver, Yearbook A.Ph.A., 7, 1918, 313; Zunz, Jl. ph. ch., 22, 1920, 361; Herzfeld and Klinger, C.A., 16, 1922, 4263.

Thyroxin.—Kendall, Yearbook A.Ph.A., 7, 1918, 312 and 8, 1919, 503; Jl. Ind. Eng. Ch., 16, 1924, 525 and Jl. Soc. Ch. Ind., 48, 1929, 608; Volweiler, Jl. Ind. Eng. Ch., 15, 1923, 909; Harington and co-workers, Jl. Soc. Ch. Ind., 45, 1926, 482, 924, 931 and 980; C.A., 23, 1929, 1631 and 5207; Baggesgaard-Rasmussen, C.A., 22, 1928, 3155.

Liquor Hypophysis.—Nelson, Jl. A.Ph.A., 13, 1924, 433.

Pituitary Gland.—Aldrich, Jl. Am. Ch. Soc., 37, 1915, 203; Pittenger and Vanderkleed, Jl. A.Ph.A., 6, 1917, 31; McNeil, Ph. Jl., 98, 1917, 295; Dudley, A.J.P., 92, 1920, 275; Abel, Jl. Ind. Eng. Ch., 16, 1924, 1031; Kamm and co-workers, Jl. Am. Ch. Soc., 50, 1928, 513; Cushing, C.A., 25, 1931, 3396.

Tethelin.—Robinson, Jl. Biol. Ch., 24, 1916, 397 and 409; Ewe, A.J.P., 91, 1919, 349.

Sex Hormones.—Doisy and co-workers, Jl. A.M.A., 81, 1923, 819; Jl. Soc. Ch. Ind., 49, 1930, 840B; C.A., 25, 1931, 5458; Jl. Soc. Ch. Ind., 51, 1932, 961B; Raab, C.A., 24, 1930, 5877; Junkmann, C.A., 25, 1931, 2469; Schoeller and Goebel, C.A., 26, 1932, 171; Butenandt and co-workers, C.A., 26, 1932, 4635; Science Supp., 75, Apr. 8, 1932, 9; Marrian and co-workers, Jl. Soc. Ch. Ind., 51, 1932, 277T; C.A., 26, 1932, 3269; Science, 74, 1932, 547; Burn, Quart. Jl. Ph., 1, 1928, 509 and 5, 1932, 190; Cook and co-workers, Science Supp., 77, Jan. 20, 1933, 8.

Insulin.—Banting and Best, Jl. Soc. Ch. Ind., 41, 1922, 537 R; Macleod, Am. Dr., 71, May, 1923, 37; Banting, Campbell and Fletcher, C.A., 17, 1923, 1502; Anon., A.J.P., 95, 1923, 369; Allen, C.A., 17, 1923, 814; Best and Scott, C.A., 18, 1924, 94 and 880; Jl. Ind. Eng. Ch., 17, 1925, 238; Fairchild, Jl. Ind. Eng. Ch., 16, 1924, 41; Carr, Jl. Soc. Ch. Ind., 43, 1924, 228T; *ibid.*, 45, 1926, 750; Dudley, *ibid.*, 43, 1924, 654B; Cruto, *ibid.*, 43, 1924, 965B; MacLeod, C.A., 18, 1924, 2531; Renshaw, Jl. Soc. Ch. Ind., 44, 1925, 95T; Abel, A.J.P., 95, 1926, 370; Funk, Science, 63, 1926, 401; Shonle, Jl. Frank. Inst., 201, 1926, 639; du Vigneaud and co-workers, C.A., 22, 1928, 452 and 2177; Ostling, C.A., 23, 1929, 236; Svedberg, Jl. Am. Ch. Soc., 53, 1931, 2657; C.A., 25, 1931, 2746; Marshall and Wiesner, Pract. Dr., 49, Sept., 1931, 34; Freudenberg and Dirscherl, C.A., 26, 1932, 738; Charles and Scott, C.A., 26, 1932, 3327; Jensen, C.A., 26, 1932, 4340; Clark, Science Supp., 75, June 3, 1932, 10.

Insulin Substitutes.—(Synthalin) Sevringhaus, Yearbook A.Ph.A., 17, 1928, 782; Weitz, C.A., 22, 1928, 3263; Bertram, C.A., 23, 1929, 200; Parise, C.A., 23, 1929, 2758. (Myrtillin) Allen, Yearbook A.Ph.A., 16, 1927, 150; Watson, C.A., 23, 1929, 197; Jorgensen and Lynn, Jl. A.Ph.A., 24, 1935, 389.

Cortin.—Hartman and co-workers, C.A., 25, 1931, 3044; Science, 73, 1931, 621 and 75, 1932, 330.

Suprarenal Glands.—Abel, A.J.P., 52, 1904, 292; Beckwith, Jl. A.Ph.A., 3, 1914, 1547.

Epinephrine.—(Structure) Pauly, B., 36, 1903, 2944 and 37, 1904, 1388; Abel, A.J.P., 75, 1903, 301; Sohn, Ph. Jl., 78, 1907, 623. (Manufacture) Takamini, A.J.P., 52, 1904, 974. (Synthesis) Stolz, B., 37, 1904, 4149; Bottger, C.A., 3, 1909, 901; Flächer, C.A., 3, 1909, 1889.

Oxgall.—(Constituents) Gobley, Jl. de ph. et ch., [3], 30, 1856, 241; Lassar-Cohn, B., 26, 1893, 146; Maly, A., 181, 1876, 106; Kuester, C.A., 7, 1913, 1494 and 11, 1917, 2681; Wieland and co-workers, C.A., 16, 1922, 3638 and 24, 1930, 5761; Schenck, C.A., 18, 1924, 3601 and 22, 1928, 2361. (Uses) Obst, C.A., 25, 1931, 1112. (Tests) Pettenkofer, A.J.P., 17, 1845, 114.

Purified Oxgall.—Wiegand, A.J.P., 32, 1884, 347.

Liver Therapy.—Minot and Murphy, Jl. A.M.A., 87, 1926, 470; *ibid.*, 89, 1927, 759; Collip, C.A., 22, 1928, 2807; Howell, C.A., 22, 1928, 2953; Anon., Nat. Dr., 59, 1929, 250; Dakin and co-workers, Ph. Era, 68, Feb., 1931, 34; Castle and Morris, Ph. Jl., 127, 1931, 50; Podolsky, Pract. Dr., 49, March, 1931, 17; Keefer and co-workers, C.A., 25, 1931, 1903; Castle, A.J.P., 108, 1936, 55.

CHAPTER LII

BACTERIOLOGY AND ITS PHARMACEUTICAL APPLICATIONS

Historical.—In 1659 Kircher and in 1675 Leeuwenhoek saw and described the micro-organisms that we now know as bacteria. These microscopic growths were further studied by Mueller (1774), Scheiden (1838) and by Ehrenberg (1838) the latter designating a particular form of these by the word "bacteria." Cohn (1876) used the word "bacillus." In 1855, Pollenden reported the presence of bacilli in the blood of animals dead of anthrax and in 1863 Davaine proved the connection between these bacilli and the disease. In 1880 Eberth discovered the typhoid bacillus and in 1882 Koch discovered the bacillus of tuberculosis. These discoveries, followed by others, established the fact of bacterial infection which was also studied by Pasteur (1879–1884), leading to the latter's brilliant work on rabies.

Koch, Weigert, and others (1880) studied the culture of bacteria and their staining, thus simplifying their identification.

Pasteur's work also included research on protective inoculations, which brought as practical results the discovery of diphtheria antitoxin by von Behring in 1893.

Bacteriology being a science in itself cannot be adequately discussed in this book, so, for details, the reader is referred to the textbooks mentioned in the Bibliography. Of these, an older book (Sternberg-Magnin,

1884) is mentioned; first because it is one of the earliest books on bacteriology and secondly because it has a bibliography of 712 references, giving practically all of the work done up to that time.

In this chapter it can only be said that bacteria or other micro-organisms produce a number of our most virulent diseases; that these diseases may be identified by a study of the specific micro-organisms; that many diseases are now prevented or cured by the use of antitoxins, serums, and other bacteriological products, and that tests for immunity to various diseases can be made upon individuals by the use of bacterial products. Bacterial identification is clearly beyond the limits of this book so in this chapter will be briefly considered:

(*a*) Treatment of disease by sera and vaccines.
(*b*) Description and application of the tests for immunity.
(*c*) Description of the official biological products of the U.S.P. XI.

BIOLOGICAL PRODUCTS AND SPECIFIC IMMUNIZATION

General Discussion.—The span of human life has been lengthened largely because of the progress in determining the cause of diseases resulting from the invasion of bacteria and providing preventive and curative methods in combating them. The progress in this field would never have attained the heights it has today if smallpox, typhoid, and the plague were still unconquered. The rapid means of communication and the congested life in cities serve to spread these diseases so quickly that travel would become stagnated and life in cities a hazardous existence, were it not for the methods devised to prevent contagion.

Most outstanding among the early discoveries in the field of immunization by biological products are those of Jenner, Pasteur, and von Behring. To Jenner is given the credit for a means of preventing one of the great scourges of mankind—smallpox; to Pasteur for overcoming rabies; and to von Behring for the conquest of diphtheria.

In spite of these great contributions to the prevention and treatment of disease, the early hopes that all disease could be overcome by similar methods has not by any means been fulfilled. Various vaccines, serums, and viruses have been tried in diseases where it would appear they might have been of value from a theoretical standpoint, but practically, such has not been the case. Many physicians have made unreasonable requirements of a vaccine, have expected a vaccine to absolutely prevent a disease, and a serum to produce a positive cure or else be considered a failure. Many good products are erroneously neglected on this account. In many cases it is not the product which is at fault but rather the lack of knowledge as to proper dosage, indications and contraindications, and a lack of proper care of the products in the physician's office, or perhaps in the pharmacy. Too much should not be expected of biological products. If they aid at all in treatment or prevention of disease, certainly they are valuable additions to medical science.

Brief Consideration of the Principles of Immunization.—A. *Natural immunity* to disease is an inherent power peculiar to species of animals, races of people, and to individuals. It is a resistance to certain pathogenic bacteria and their toxins, brought about in all probability as a result of a long-continued struggle against the invading parasites.

B. *Acquired immunity.* In this type of immunity the resistance to disease is not inherent as in natural immunity, but may be acquired in various ways, as:

(*a*) By having an attack of the disease;

(*b*) By artificial immunization with attenuated bacteria or bacterial products.

By having an attack of the disease. Throughout the course of an illness a struggle takes place between the bacteria and their toxins and the defensive forces of the individual. Immune substances, called antibodies, are built up in the blood serum, which are capable of neutralizing the toxins, and also of destroying the bacteria themselves. The rapidity with which the individual can form these antibodies often has an important bearing on the outcome of the case. At times the struggle is long and furious, terminating either successfully for the individual or in death from overwhelming toxemia. In diseases as smallpox, typhoid fever, bubonic plague, diphtheria, poliomyelitis, and scarlet fever, an excessive amount of these immune bodies are formed, so that subsequent exposure to them is not followed by any evidence of infection in the individual. The stimulation of the body cells to produce immune substances in disease is brought about by the presence of bacteria which have gained entrance into the body tissues in one way or another.

By artificial immunization. The injection of bacteria and their products, modified in such a way that the body cells will be stimulated to produce immune substances without actually infecting the individual, constitutes the basis for the use of vaccines. In other cases the immunity is acquired by inoculation with serums containing the immune bodies, previously formed in the blood serums of animals. The immunity produced is artificial in both cases, but is more or less permanent with vaccines, whereas with serums it is temporary, as no stimulation of the body cells of the individual inoculated occurs.

Immunization by the Use of Vaccines.—The word vaccine (from the Latin "vacca," meaning "cow") in its original use implied the attenuated or weakened living virus of cowpox, which is practically a modified form of smallpox. Considerable confusion occurred when Pasteur's rabies virus and later the suspensions of killed bacteria were also called vaccines. These latter products having nothing in their preparation which would allow them to be called vaccines if the term were used in its original sense. Their biological properties would be clearly indicated if they were called bacterial antigens (an antigen being a substance that possesses immunizing properties). However, the word vaccine has today become universally applied to a great many bacterial preparations which stimulate the formation of antibodies in the blood of the injected individual, and if used with that in mind, the term "vaccine" has a definite meaning. Thus we have official vaccine virus, typhoid vaccine, toxoid, rabies vaccine, BCG vaccine, although they are all very different products.

The most important varieties of vaccines used today are:

1. Bacteria killed by heat or chemicals and suspended in salt solution; *e. g.*, typhoid vaccine, dysentery vaccine, catarrhal vaccines.
2. Living bacteria. Very little used in United States.
3. Ultramicroscopic bacteria (called viruses) modified by passage through some animal; *e. g.*, smallpox and rabies viruses.
4. Bacteria modified by growth on unfavorable media; *e. g.*, BCG vaccine against tuberculosis, anthrax vaccine.
5. Bacterial products modified in various ways; *e. g.*, toxin-antitoxin, toxoid, scarlet fever toxin.

Classification of Vaccines.—*Autogenous Vaccines.*—These are made from germs taken from the patient's own infected tissues and used in the treatment of the same patient.

Stock Vaccines.—Germs are taken from clinical cases and grown upon culture media until a strain is obtained that will produce stimulation of immune substances. These strains are then grown on a large scale and constitute the majority of the vaccines used today. Usually a single strain is specific, as in typhoid vaccine, but in the case of catarrhal vaccines a number of different bacteria are combined. These are called mixed stock vaccines, and are used with the hope that immunity to respiratory infections may be produced by one or more of the bacteria contained in the vaccine.

The Vaccine Container.—Vaccines are usually marketed in sterile glass vials with rubber caps, making it possible to remove desired amounts of the vaccine without danger of contamination to the remaining portion. The name and number of cubic centimeters in each vial, with data as to strength or composition, is placed on the label.

Method of Administering Vaccines.—1. By hypodermic injection, either subcutaneously or intramuscularly, the former being the most widely employed method.

2. By mouth. Oral vaccines are enteric coated so that they will pass through the stomach and be set free in the intestines. This form of administration is being used successfully in the prevention of typhoid fever. It is claimed that the immunity developed is as high as with hypodermic injection, and that there is little systemic reaction.

3. By local application. Local vaccines are applied in the form of wet dressings or are injected directly into the tissues infected. Their use in this country has not been attended by the success claimed for them in Europe.

Dosage of Vaccines.—It is exceedingly difficult to measure the dose accurately for all individuals, and this has been the reason for most of the failures in the use of vaccines. Attempts are made to give measured amounts of vaccine containing a known number of attenuated bacteria at stated intervals. While this is valuable in many cases, and has produced excellent results, it is by no means justifiable in all cases. Vaccines should be given according to reactions produced, and at intervals depending upon those reactions. Small doses frequently given and increased in such a manner that severe systemic reactions are avoided will often produce results in those cases where failures have occurred from attempts to follow a prescribed routine dosage.

Immunization by the Use of Serum.—Serum therapy came into prominence with the discovery by von Behring that the toxin of the diphtheria bacillus, when injected into an animal, produced in the blood serum of that animal substances which would neutralize the toxin. By the injection of this animal serum containing the immune substances he found that a child sick with diphtheria recovered quickly from the disease. The patient will usually produce the immune substance himself, but often not rapidly enough to neutralize the amount of poison formed and the animal serum contributes additional immune substances which combine with and render inert the toxin in the blood. Unlike vaccines, no stimulation of the patient's cells takes place by the injected serums; therefore, the immunity produced by serums is not lasting. The immune substances not used up by combination with the toxin gradually disappear from the blood and in a few weeks are lost entirely.

Serum therapy appears to be of most value in those diseases in which soluble toxins of the bacteria are of importance, as diphtheria, tetanus, and streptococcic infections.

Source of Bacterial Serums.—From animals immunized against the toxin or bacteria themselves. Horse serum is most extensively used as there are few diseases of horses that are communicable to human beings, and in addition, the horse can furnish large amounts of serum. Objection to the use of horse serum is due to the toxic effect that is produced in certain individuals following the injection of large amounts of therapeutic serum. This objection has been somewhat overcome by concentrating the serum and removing much of the harmful protein elements which have no immunizing value anyway.

Bovine serum has been advocated to overcome the disadvantage of horse serum, as it appears less toxic. However, some people may be sensitive to bovine serum and subsequent injections would have to be given carefully.

Sheep, goats, rabbits, and other animals have been used for the production of immune serums, but the small amounts produced make them unsatisfactory for commercial purposes.

Human serum is sometimes of value in those diseases against which animal immunization is not always successful. Serums of patients convalescent from infantile paralysis, measles, and mumps, have been used in the treatment of these diseases and also in the prophylaxis during an epidemic. The blood serum of normally immune persons may be of advantage in the treatment of measles, but must be given in larger amount than convalescent serums. The danger of transmitting other diseases and the large amount of serum required makes human serums unpopular for general use.

Classification of Serums.—*Antitoxic serum* is produced by the injection of an animal with increasing doses of the soluble toxin of the germ. Diphtheria, scarlet fever, tetanus, erysipelas, botulism, and gas gangrene have been successfully treated by antitoxic serums prepared in this manner. These antisera act by combining with the toxin in the blood of the patient, rendering it inert.

Antibacterial serum is produced by injection of the animal with successive doses of the bacteria. The immune substances thus formed act by enhancing phagocytosis and destroy bacteria, and are known as opsonins, precipitins, agglutinins, anti-aggressins. Pneumonia, streptococcic infection and spinal meningitis have been aided by the use of this type of serum. They are not as valuable as antitoxic serums, but have done much to retard the mortality in these conditions.

Mixed serum contains both antitoxic and antibacterial immune bodies. The serum used in the treatment of scarlet fever is of this type, and has given excellent results in some hands.

Standardization of Serums.—Antitoxins are standardized in terms of "antitoxic units" against standard units furnished by the National Institute of Health of the U. S. Public Health Service.

Briefly the diphtheria antitoxic unit is determined in the following manner:

The toxin (as the poisonous product of the culture is called) is prepared and administered to a number of guinea-pigs each weighing 250 Gm. The smallest amount of toxin killing the guinea-pigs within four days is the Minimum Lethal Dose (M. L. D.). One hundred times this quantity of toxin is mixed with various amounts of the antitoxin and is administered to a second batch of guinea-pigs. The smallest amount of the antitoxin which prevents the hundred-fold dose of toxin from killing the guinea-pigs represents the antitoxic unit. One hundred times this volume of antitoxic serum would represent 100 units. Antitoxic units for other antitoxins are determined in somewhat the same manner.

Of great importance is the insuring against deterioration of the serum below that of the standard. This is accomplished by increasing the potency considerably above the standard shown on the label. The antitoxin can then be used over a period of time with confidence that it will contain at least the required number of units.

Antibacterial serums cannot be standardized in such units, but tests for sterility and potency are made on laboratory animals to insure a relatively high content of antibodies.

Clinical Uses of Serums.—For therapeutic purposes relatively large doses of serums should be given as soon as possible after a diagnosis is made. When there is doubt as to the size of the dose of antitoxin to be used, it is usually better to give the larger dose. The danger of serum reaction must always be kept in mind.

For prevention or prophylaxis smaller doses are given when exposure has been known to have taken place. Diphtheria, tetanus, and measles can frequently be prevented by this method. The immunity produced is only temporary and subsequent exposure will not be affected by such inoculations.

Serum Reactions.—The injection of serum for either prophylaxis or treatment is occasionally attended by severe and sometimes fatal reactions. These are due to the fact that certain individuals are naturally sensitive to the serum of animals from which the serums are made. It should be determined before giving a serum whether or not the patient has ever suffered from asthma or allergic symptoms, and if he has received serum at any previous time. Should such a history be elicited, the patient must be tested for sensitivity before injecting the serum. A marked urticarial wheal at the site of the injection of a small amount of serum should be a warning that desensitizing is necessary. This can be accomplished by successive injections of small amounts of the serum gradually increasing the quantity until it is felt all danger of shock is passed. In a grave case of diphtheria, the danger of reaction should not be a reason for failing to give a curative dose of antitoxin, as records of death from injections in such cases are practically nil.

Serum treatment given with due care and precaution is one of the greatest accomplishments in scientific medicine today. It is correct from a theoretical standpoint, and its practical value has been demonstrated by the drop in mortality of diphtheria, tetanus, and other infections.

Important Factors Concerning Biologicals in General.—The rigid regulations regarding the manufacture and sale of biological products set up by the National Institute of Health insures the medical practitioner of safe and valuable agents. A license to manufacture these products must be obtained from the Treasury Department through the U. S. Public Health Service. The laboratory, personnel, equipment and methods of preparation must meet the requirements of the National Institute of Health before a firm can engage in the production of biologicals.

Failure to obtain good results from the use of biological products is often due to the lack of adequate knowledge of their proper care. As a general rule, vaccines and serums should be kept at temperatures between 2° and 8° C., preferably at the lower temperature. Exposure to room temperature for any length of time will readily destroy smallpox virus, rabies virus, and diphtheria toxin-antitoxin. Serums are somewhat more stable and may remain potent for several years at even 50° to 60° C., although this is not advisable in all cases. Allowance is made for the deterioration of antitoxins by standardization to a point in excess of the minimum number of units shown on the label. In this manner the potency of such products is assured until the date of expiration, beyond which the manufacturer does not guarantee the antitoxin strength.

The outside label of the package containing the biological product must indicate the name of the product, the name, address, and license number of the manufacturing firm, the minimum potency, the date of manufacture or the expiration date. If there is no U. S. Standard for the product, such announcement should be made on the label.

Tests for sterility, purity, toxicity, and potency are conducted by the firms which make biologicals and also by the National Institute of Health.

In the case of all biological products the clinical value of any product is not evaluated by the National Institute of Health.

Bacteriophage and Its Application.—Largely due to the work of d'Herelle it is believed that there exists an ultramicroscopic or filtrable virus which acts as an endoparasite upon bacteria and is capable of destroying living cultures of bacteria under certain conditions. By the introduction of this bacteriophage into the body of an individual suffering from a disease germ against which the bacteriophage is active d'Herelle claims that the germs are quickly destroyed. Good results have been reported in the treatment of diseases such as typhoid fever, bacillary dysentery, cholera, plague, colon bacillus infections, and staphylococcus infections.

The bacteriophage is prepared in several ways for administration and in the case of staphylococcus infections it is applied in the form of wet dressings or injected directly into the diseased tissue.

Although there is considerable difference of opinion regarding the nature of bacteriophage and its action in the tissues, nevertheless it has opened up a new field in immunological therapy and appears to be of considerable value in the treatment of certain diseases. It is of utmost importance that the bacteriophage come into direct contact with the bacteria it is intended to destroy. Thus, the method of application or administration of bacteriophage virus must be suited to the type of infection in the tissues in order to obtain the good results that have been reported by d'Herelle and others.

Nonspecific Protein Therapy.—For many years it has been recognized that considerable benefit results from the injection of various substances in the treatment of diseases in which it would appear, from our knowledge of immunity, that such benefit is not to be expected. Vaccines, normal horse serum, normal human serum, sterile milk, egg-albumen, and many other substances, which are alike in that they are of a protein nature, when injected give rise to reactions in the body, the severity depending upon the amount of the material that is injected.

Apparently they do not stimulate the formation of immune substances that are specific for the material injected but rather cause an increase in the production of immune substances that are being formed in the blood at the time the nonspecific substances are injected. It is also noted that there is an increase in the white blood cell count and that phagocytosis may be increased thereby. Whatever is the exact explanation of the phenomenon which occurs as the result of this form of therapy the benefit does not come entirely from a specific reaction. In all probability there is a "protein shock" produced which sets free already formed immune bodies and at the same time stimulates the formation of new antibodies. There is no exact dosage for substances injected in nonspecific protein therapy and unless carefully carried out, treatment may be accompanied with a considerable element of danger to the individual. Unfortunately, there are no clearly defined or scientific indications for much of this type of therapy but in some hands it has given remarkable results.

ANTITOXINS

ANTITOXINUM DIPHTHERICUM—Diphtheria Antitoxin

(**Antitox. Diph.**—Purified Antidiphtheric Serum, Concentrated Diphtheria Antitoxin, Refined Diphtheria Antitoxin, Antidiphtheric Globulins)

Diphtheria Antitoxin is a sterile aqueous solution of antitoxic substances obtained from the blood serum or plasma of a healthy animal of the genus *Equus*, which has been immunized against diphtheria toxin. After the serum or plasma from the immunized animal has been collected, the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in freshly distilled water. Sodium chloride and a preservative are then added and the solution is filtered through a bacteria-excluding filter. Diphtheria Antitoxin has a potency of not less than 500 antitoxic units per cc.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Diphtheria Antitoxin is a transparent or slightly opalescent liquid of a faint brownish, yellowish or greenish color. A very slight odor of the preservative and a granular deposit may be present but these are of no consequence. The total solids are not more than 20 per cent. It must be free from toxin and not contain more than 0.5 per cent phenol or 0.4 per cent cresol.

Potency.—The unit of potency is that of the Standard Diphtheria antitoxin distributed by the National Institute of Health of the U. S. Public Health Service.

Expiration Date.—This date is one year from issue by the manufacturer if at that time the antitoxin contained an excess of 20 per cent units over the stated minimum potency, two years if 30 per cent over, three years if 40 per cent and four years if 50 per cent over.

Remarks.—Diphtheria Antitoxin is prepared from the serum of healthy horses which have been immunized against diphtheria toxin. The toxin is obtained by growing diphtheria bacilli in a special nutrient bouillon and injecting successively larger doses of this toxin into a horse at predetermined intervals until its resistance has been built up to a high degree by the production of antitoxin in its own blood. Some quantity of blood is removed from the jugular vein and the serum allowed to separate. Antitoxic globulins are then removed from the serum by chemical precipitation and are dissolved in distilled water. Sodium chloride and a preservative are added and the solution filtered to remove any bacteria that might be present. After tests for sterility and potency the solution is placed in glass containers or syringes for dispensing purposes.

In the U.S.P. IX crude, purified, and dried forms of antitoxin were recognized. However, the U.S.P. X and XI, following modern developments in serum treatment, recognizes only the purified antitoxin, which is practically free from other inert and harmful serum constituents. It consists of the antitoxic globulins dissolved in distilled water and standardized.

Administration and Dosage.—By subcutaneous, intramuscular or intravenous injection. Therapeutic dose: 10,000 units (U.S.P.) average dose. Prophylactic dose: 1000 units (U.S.P.).

In the treatment of diphtheria it is not unusual to give much larger doses of antitoxin. In severe cases 50,000 to 75,000 units is considered good practice and there are many who advocate the larger dose as it lessens the danger of having to give several small doses.

ANTITOXINUM SCARLATINÆ STREPTOCOCCICUM—Scarlet Fever Antitoxin

(Antitox. Scarlat. Streptococ.—Scarlet Fever Streptococcus Antitoxin, Refined Scarlet Fever Antitoxin, Concentrated Scarlet Fever Antitoxin, Anti-Scarlet Fever Globulins)

Scarlet Fever Antitoxin is a sterile aqueous solution of antitoxic substances obtained from the blood serum or plasma of a healthy animal of the genus *Equus* which has been immunized against the toxin or toxin-like substance produced by the streptococcus regarded as causative of scarlet fever. After the serum or plasma from the immunized animal has been collected, the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in freshly distilled water. Sodium chloride and a preservative are then added and the solution is filtered through a bacteria-excluding filter. Scarlet fever antitoxin has a potency of not less than 400 antitoxic units per cc.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Scarlet Fever Antitoxin is a transparent or slightly opalescent liquid of a faint brownish, yellowish or greenish color. A very slight odor of the preservative and a granular deposit may be present but these are of no consequence. It must be free from toxin and must not contain more than 0.5 per cent phenol or 0.4 per cent cresol.

Potency.—Scarlet Fever Antitoxin has a potency of not less than 400 antitoxic units per cc. The unit of potency is that of the standard Scarlet Fever Antitoxin distributed by the National Institute of Health. (One unit of Scarlet Fever Antitoxin [N.I.H.] is the least amount of antitoxin which completely neutralizes 50 skin test doses of scarlet fever toxin.) One skin test dose of scarlet fever toxin will give an area of erythema of at least 1 cm. in diameter when injected intradermally in a susceptible person.

Expiration Date.—This date is one year from the date of issue by the manufacturer if the antitoxin contains an excess of 20 per cent over the minimum of potency, two years if 30 per cent, three years if 40 per cent, four years if 50 per cent excess.

Remarks.—Scarlet Fever Antitoxin is prepared from the serum of healthy horses which have been immunized against scarlet fever toxin. The toxin is obtained by growing the streptococcus of scarlet fever in a special broth. Increasingly larger doses of this toxin are injected into the animals at daily intervals until sufficient antitoxins have been built up in the blood. The horse is then bled and the serum separated. Antitoxic globulins are removed from the serum by precipitation and dissolved in distilled water. A preservative is added and after tests for potency and sterility the antitoxin is placed in glass containers for dispensing purposes.

Administration and Dosage.—By subcutaneous, intramuscular, and intravenous injection. Therapeutic dose: 6000 units. Prophylactic dose: 2000 units.

ANTITOXINUM TETANICUM—Tetanus Antitoxin

(Antitox. Tet.—Purified Antitetanic Serum, Concentrated Tetanus Antitoxin, Refined Tetanus Antitoxin, Antitetanic Globulins)

Tetanus Antitoxin is a sterile aqueous solution of antitoxic substances obtained from the blood serum or plasma of a healthy animal of the genus *Equus*, which has been immunized against tetanus toxin. After the serum or plasma from the immunized animal has been collected, the antitoxin-bearing globulins are separated from the other constituents of the serum or plasma and dissolved in freshly distilled water. Sodium chloride and a preservative are then added and the solution is filtered through a bacteria-excluding filter. Tetanus Antitoxin has a potency of not less than 300 antitoxic units per cc.*

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Tetanus Antitoxin is a transparent or slightly opalescent liquid of a faint brownish, yellowish or greenish color. It may have a slight odor of the preservative.

Potency.—Tetanus Antitoxin has a potency of not less than 300 antitoxic units per cc. The unit of potency is that of the Standard Antitoxin distributed by the National Institute of Health. (One unit of Tetanus Antitoxin is 10 times the least amount of antitoxin which will protect a 350-gram guinea-pig from one L+ dose of tetanus toxin for at least four days. The L+ dose of toxin being the smallest amount which will kill a 350-gram guinea-pig on the fourth day in the presence of .1 unit of Standard Antitoxin furnished by the National Institute of Health.)

Expiration Date.—This is the same as for Diphtheria Antitoxin.

Remarks.—The U.S.P. IX recognized three forms of antitoxic serum—the crude, purified, and dried. The present U.S.P. XI recognizes only the purified serum which contains the antitoxic globulins that have been precipitated from the serum and dissolved in distilled water. It is thereby freed from many of the inert and harmful serum constituents.

Administration and Dosage.—By subcutaneous, intravenous, and intraspinal injection. Therapeutic dose: 20,000 units. Prophylactic dose: 1500 units, subcutaneously.

ANTIBACTERIAL SERUMS

SERUM ANTIMENINGOCOCCICUM—Antimeningococcic Serum

(**Serum Antimeningococ.**—Antimeningococcus Serum, Meningococcus Serum, Meningitis Serum)

Antimeningococcic Serum is obtained from the blood of an animal of the genus *Equus* immunized with cultures of the several types of meningococci (*Neisseria intracellularis*) which prevail in the United States.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Antimeningococcic Serum is a yellowish, clear or slightly turbid liquid with a faint odor of the preservative. It may have a fine granular deposit at times.

Potency.—Antibacterial sera cannot be standardized as can antitoxins. Various serologic and protective tests are made upon animals to insure a high content of the specific antibodies.

Expiration Date.—This date is stated on the package by the manufacturer. Beyond the date so stated the product is not expected to retain its potency.

Remarks.—The discovery that the meningococcus produces an extracellular toxin has led to use of an antitoxin in the treatment of this disease. Good results have been obtained and it is felt by some that the benefit derived from the antibacterial serum is probably due to the antitoxic content of the serum which heretofore had not been suspected.

Administration and Dosage.—By subcutaneous, intravenous, and intraspinal injection. Therapeutic dose: 20 cc. average dose.

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* *The International Unit.*—The unit of potency for Tetanus Antitoxin referred to in this Pharmacopœia is usually spoken of as the "American Unit"; it is approximately double the strength of the "International Unit" established by the Permanent Standards Commission of the Health Organization of the League of Nations.

SERUM ANTIPNEUMOCOCCICUM-I—Antipneumococcic Serum, Type I

(**Serum Antipneumococ.-I**—Antipneumococcus Serum, Type I, Pneumonia Serum, Type I)

Antipneumococcic Serum, Type I, is obtained from the blood of an animal of the genus *Equus* which has been immunized with cultures of a pneumococcus (*Diplococcus pneumoniæ*) of the variety known as "Type I."

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Antipneumococcic Serum, Type I, is a yellowish, clear or slightly turbid fluid with a faint odor of preservative. It may have a fine granular deposit at times.

Potency.—Same as for Antimeningococcic Serum.

Expiration Date.—This date is stated on the package by the manufacturer.

Remarks.—Type I pneumonia is apparently caused by a single strain of the *Diplococcus pneumoniæ* and accounts for about one third of the cases of lobar pneumonia. Special typing serum is available for determining the type of pneumonia. Mortality in this type of pneumonia has been greatly reduced since the introduction of Type I serum.

Administration and Dosage.—By subcutaneous, intravenous, and intraspinal injection. Therapeutic dose: 30 cc. average dose.

TOXINUM DIPHTHERICUM DETOXICATUM—Diphtheria Toxoid

(**Toxin. Diphtheric. Detox.**—Diphtheria Anatoxin, Anatoxin-Ramon)

Diphtheria Toxoid is a sterile aqueous solution of the products of growth of the diphtheria bacillus (*Corynebacterium diphtheriæ*) so modified by special treatment as to have lost the ability to cause toxic effects in guinea-pigs but retaining the property of inducing active immunity. The toxicity of the Diphtheria Toxoid shall be so low that five times the dose for the adult human does not cause either local or general symptoms of diphtheria poisoning in a guinea-pig within thirty days after its injection into the animal. The antigenic value shall be such that the initial dose for the human shall protect at least 80 per cent of guinea-pigs, six weeks after injection, against 5 minimum lethal doses each of diphtheria test toxin. Some specimens are concentrated and purified by precipitating and washing the active portion of the detoxified material. Such concentrated and purified specimens must be capable, when injected into guinea-pigs, of inducing the production of diphtheria antitoxin of such potency as is prescribed by the National Institute of Health of the United States Public Health Service.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Diphtheria Toxoid is a clear, brownish-yellow or turbid liquid having a faint odor of broth or preservative. Unconcentrated specimens are usually clear.

Remarks.—Diphtheria toxoid is prepared by growing the *Corynebacterium diphtheriæ* on broth medium until a maximum amount of the toxin is produced. The bacilli are filtered out and 0.4 per cent formalin added to the filtered toxin. The formalized toxin is then incubated at 37° C. until it becomes atoxic. (Toxoid precipitated by alum has a coarse flocculent precipitate giving it a milky white suspension.)

Administration and Dosage.—By subcutaneous injection. Prophylactic: 1 cc. given at an interval of two to four weeks until two doses have been administered.

DIAGNOSTIC TOXINS

TOXINUM DIPHTHERICUM DIAGNOSTICUM—Diphtheria Toxin for the Schick Test

(Toxin. Diphtheric. Diagnost.—Schick Test Toxin)

Diphtheria Toxin for the Schick Test is a solution of the toxic products of growth of the diphtheria bacillus (*Corynebacterium diphtheriæ*).

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Diphtheria Toxin for the Schick Test is a clear, transparent liquid.

Potency.—One-fiftieth of the M. L. D. (Minimum Lethal Dose) of Diphtheria Toxin suspended in 0.1 cc. of normal salt solution, the M.L.D. of the toxin being the smallest amount of toxin that will cause the death of a guinea-pig weighing 250 Gm. in four days.

Expiration Date.—The date beyond which the product is not guaranteed by the manufacturer to retain its potency is stated on the outside of the package.

Remarks.—In practical application of the Schick test the toxin is injected intradermally about the middle of the left forearm. The formation of an area of erythema at the site of injection which persists for several days and gradually fades is considered a positive reaction. It shows that the individual does not have enough antitoxin to neutralize the one-fiftieth M. L. D. of toxin. A negative test may show some redness for the first twenty-four hours after injection but this must not be confused with the positive reaction that persists for a number of days.

Administration and Dosage.—For determining susceptibility to diphtheria: intradermally 0.1 cc. of a diluted toxin which represents one-fiftieth of a minimum lethal dose.

TOXINUM SCARLATINÆ STREPTOCOCCICUM—Scarlet Fever Streptococcus Toxin

(Toxin. Scarlat. Streptococ.—Scarlet Fever Streptococcic Toxin, Scarlet Fever Toxin for Immunization and for the Dick Test)

Scarlet Fever Streptococcus Toxin is a sterile solution in beef broth of certain products including a soluble toxin, resulting from the growth in the broth of suitable strains of hemolytic streptococci (*Streptococcus scarlatinæ*).

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Scarlet Fever Streptococcus Toxin is a clear, transparent liquid having an odor of broth from which it is prepared.

Potency.—This is expressed in skin test doses. The skin test dose is that quantity of toxin that will give a positive reaction in all persons susceptible to scarlet fever and a negative reaction in persons immune to scarlet fever, when injected intradermally.

Remarks.—In the practical application of the Dick test the Scarlet Fever Streptococcus Toxin is injected intradermally on the flexor surface of the middle of the forearm. The formation of an area of erythema 1 cm. in diameter at the site of injection within twenty-four hours is a positive reaction. However, this area of redness disappears rapidly and within twenty-four hours may have disappeared entirely.

Administration and Dosage.—Intradermally; 0.1 cc. of the dilution—one skin test dose. For active immunization: usually a series of five hypodermic injections at intervals of four or five days. First dose, 500 skin test doses. Second, 2000; third, 8000; fourth, 25,000; fifth, 80,000 skin test doses.

TUBERCULIN

TUBERCULINUM PRISTINUM—Old Tuberculin

(**Tuberculin. Prist.**—Tuberculin-Koch, Concentrated Tuberculin, Crude Tuberculin)

Tuberculin is a sterile solution in a special liquid culture medium of the soluble products of growth of the tubercle bacillus (*Mycobacterium tuberculosis*) and should contain about 50 per cent of glycerin.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Old Tuberculin is a clear, brownish liquid having a characteristic odor and readily soluble in water.

Potency.—The potency of Old Tuberculin is determined by animal testing. There is no U. S. standard of potency.

Remarks.—Cultures of the tubercle bacillus are grown in bouillon containing 5 per cent glycerin for three to six months. The entire culture is concentrated over a steam bath to one tenth the volume and filtered through a porcelain filter to remove the organisms. The final filtrate constitutes Old Tuberculin. More glycerin is added until it contains at least 50 per cent of glycerin.

Administration and Dosage.—By intracutaneous injection. Diagnostic test dose: 0.001 cc.

VACCINES

VACCINUM RABIES—Rabies Vaccine

(**Vac. Rabies**—Antirabic Vaccine, Antirabic Virus, Pasteur Treatment, Pasteur Prophylactic)

Rabies Vaccine is a sterile suspension of the attenuated, diluted, dried or dead, fixed virus of rabies. The virus is contained in the tissue of the central nervous system of an animal suffering from, or dead of, fixed virus rabies infection.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

Rabies Vaccine is a somewhat turbid, whitish liquid with a slight odor of the preservative.

Potency.—There is no U. S. standard of potency. It is determined by various laboratory tests on animals.

Expiration Date.—The date beyond which the vaccine may not be expected to retain its potency is placed on the label.

Remarks.—Rabies Vaccine is prepared by inoculating rabbits with "street virus" until the disease becomes so virulent for the rabbits that they die regularly on the seventh day. This is called "fixed virus" as it cannot be increased in virulence for the rabbits. However, it was found that the fixed virus decreased in virulence for dogs and humans at the same time it was increasing in virulence for rabbits. The tissue of the central nervous system of the rabbits which contains this virus is dried over potassium hydroxide for a certain length of time in order to further reduce its virulence. An emulsion is made of the central nervous tissue so treated and placed in sterile glass containers.

Most methods of preparation of Rabies Vaccine today are modifications of the original Pasteur method. In the Semple method the virus is killed with phenol and a low degree of heat. The advantages of this method are that the virus is dead, that the product is stable and can be stocked by pharmacists, if there is reason to do so because of unusual frequency of rabies in a given locality.

Administration and Dosage.—The usual treatment consists of fourteen hypodermic injections made on as many consecutive days and given under the skin of the abdomen.

The daily dose is the contents of the container for each of the fourteen or more days of treatment.

The vaccine should be administered as soon as possible after infliction of the suspected wound as the vaccine is chiefly a preventative for rabies and not a method of treatment.

VACCINUM TYPHOSUM—Bacterial Vaccine made from the Typhoid Bacillus

(**Vac. Typhos.**—Typhoid Prophylactic, Enteric Vaccine)

Bacterial Vaccine made from the Typhoid Bacillus is a sterile suspension of killed typhoid bacilli (*Eberthella typhi*) in physiological solution of sodium chloride or other suitable diluent. The Vaccine shall contain, in each cc., at least 1,000,000,000 typhoid organisms.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass container in which it was placed by the manufacturer.

Summarized Description.

A slightly turbid liquid with a slight odor of the preservative. On standing a granular deposit may be observed.

Potency.—Typhoid Vaccine should contain at least 1,000,000,000 organisms in each cubic centimeter. Tests for potency are made upon animals.

Generally a polyvalent vaccine is more desirable than a monovalent vaccine.

Expiration Date.—The date beyond which the potency of the vaccine is not guaranteed is stated on the label. This date is usually eighteen months from date of release of the vaccine.

Remarks.—Typhoid Vaccine is made by growing the organisms on suitable culture media. The growth is washed off with normal salt solution and by means of a shaking device made into a uniform suspension. The organisms are killed by heating or chemicals. The number of killed organisms in each cubic centimeter is then determined and the suspension diluted to the desired strength. Phenol 0.5 per cent or cresol 0.4 per cent is added as a preservative.

The United States Army uses a monovalent vaccine which has been found to cause little local or systemic reaction and still retains the same number of killed organisms as the vaccine formerly used. It has also an advantage in that the doses are reduced one half that of the former vaccine.

Administration and Dosage.—By hypodermic injection usually in the arm near the insertion of the deltoid muscle.

Prophylactic dose: 0.5 cc., 1 cc., and 1 cc. given at weekly intervals.

Oral administration of typhoid vaccine has been found to be highly efficient and obviates the objection which many have to hypodermic medication.

VACCINUM TYPHO-PARATYPHOSUM—Bacterial Vaccine made from the Typhoid Bacillus and the Paratyphoid "A" and "B" Bacilli

(**Vac. Typho-paratyphos.**—Typhoid Combined Vaccine, Typhoid-Paratyphoid Combined Vaccine, Typhoid Mixed Vaccine Prophylactic, Typhoid-Paratyphoid Prophylactic, Mixed Enteric Vaccine)

Bacterial Vaccine made from the Typhoid Bacillus and the Paratyphoid "A" and "B" Bacilli is a suspension in physiological solution of sodium chloride of killed typhoid bacilli (*Eberthella typhi*) and killed paratyphoid "A" bacilli (*Salmonella paratyphi*) and killed paratyphoid "B" bacilli (*Salmonella schottmülleri*).

The vaccine shall contain in 1 cc., at least 1,000,000,000 typhoid organisms and at least 500,000,000 of each of the paratyphoid organisms.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at the lower limit. It must be dispensed in the unopened glass containers in which it was placed by the manufacturer.

Summarized Description.

Same as for Typhoid Vaccine.

Potency.—The vaccine should contain at least 1,000,000,000 typhoid bacilli and at least 500,000,000 paratyphoid A and B bacilli.

Expiration Date.—Eighteen months from date of release of the vaccine.

Remarks.—Where there is danger of food infection as well as typhoid fever persons should receive the mixed vaccine rather than typhoid vaccine alone.

Administration and Dosage.—By subcutaneous injection as for typhoid. Prophylactic: 0.5 cc., 1 cc., 1 cc., at weekly intervals.

VACCINUM VARIOLÆ—Smallpox Vaccine

(**Vac. Var.**—Virus Vaccinicum, Glycerinated Vaccine Virus, Jennerian Vaccine, Antismallpox Vaccine)

Smallpox Vaccine consists of a glycerinated suspension of the vesicles of vaccinia or cowpox which have been obtained from healthy vaccinated animals of the bovine species. The vesicles must be removed and the vaccine must be prepared under aseptic conditions.

The vesicles must be removed from the animal at the time of maximum potency, thoroughly triturated and made into a smooth suspension with an aqueous solution of glycerin. This solution shall not be acid to bromcresol purple T.S. and not distinctly alkaline to phenol red T.S.

Storage.—Preserve and dispense Smallpox Vaccine in hermetically sealed, capillary glass tubes.

It must be kept at a very low temperature, preferably below 0° C., and never above 5° C. as it loses potency rapidly at higher, even moderate, temperatures.

Summarized Description.

Smallpox Vaccine is a thick, creamy fluid which tends to separate into clear and opaque portions.

Potency.—There is no U. S. standard of potency. However, Government supervision is so careful that companies engaged in the preparation of vaccine take great care to avoid contamination and therefore purity and potency are of a high grade. The danger of tetanus or other infections from the use of Vaccine Virus is today practically eliminated.

Expiration Date.—Vaccine Virus will keep well for many months if kept at or below freezing temperatures. The exact date beyond which the vaccine is not expected to retain its potency is designated on the label.

Remarks.—While smallpox virus has been used for over a century as a preventative for that dread disease it was first made official in the U.S.P. IX, the main object of pharmacopœial recognition being to insure a hygienic and reasonably uniform product.

In the United States the smallpox vaccine is obtained entirely from heifers that have been inoculated with seed virus originally obtained from cowpox. The heifers are subjected to careful examination and kept in quarantine for fourteen days. Each animal is thoroughly scrubbed and disinfected before being placed on the operating table. The abdomen and inner surfaces of the flanks are shaved and scarified with a knife. The seed virus is rubbed into these scarifications. In about seven to nine days vesicles which contain the virus form along the scarified marks. These are scraped off into sterile glass vessels containing glycerin and chilled. The mass is thoroughly triturated to form a smooth emulsion, strained, and after aging and testing is filled into capillary tubes.

Administration and Dosage.—By multiple puncture or multiple pressure methods through a drop of the vaccine placed on the skin of the arm over the insertion of the deltoid muscle. Female children may be vaccinated on the thigh or leg if preferred.

UNOFFICIAL PRODUCTS

In addition to the official list of biological products there are a number of preparations that have widespread use among the medical profession. In some hands these have given excellent results and are mentioned here because of their usefulness.

Antitoxins and Sera:

Gas Gangrene Antitoxin. May be used either therapeutically or as a prophylactic measure against gas gangrene intoxication.

Antistreptococcus Serum. A polyvalent serum used in streptococcus infections.

Antistreptococcus Erysipelas Serum. An antibacterial serum used in the treatment of erysipelas.

Antidysentery Serum. Used in the treatment of bacillary dysentery of the true Shiga type. It is of no value in the common types of dysentery seen here as they produce no true toxin.

Vaccines:

Acne Combined Vaccine. Used in acute and chronic acne.

Catarrhal Vaccine. Used in prevention and treatment of acute and chronic respiratory infections.

Gonococcus Vaccine. Used in the treatment of chronic gonorrhea.

Colon Bacillus Vaccine. Used in subacute and chronic infections due to the *B. Coli.*

Pertussis Vaccine. For the treatment and prevention of whooping cough.

Plague (Haffkine's) Vaccine. For the prevention of the bubonic plague.

Toxoid:

Tetanus Toxoid. For the prevention of tetanus by active immunization.

Toxoid (alum precipitated). A refined toxoid in which the active antigenic substances are precipitated with aluminum-potassium sulfate. Used in the prevention of diphtheria and requires only one dose for immunization.

PARENTERAL MEDICATION

Under this heading we include the administration of drugs by a route other than through the alimentary canal and usually by injection. In the administration of drugs by injection, we may have recourse to *intradermal injections; hypodermic* or *subcutaneous injections; intramuscular injections; intravenous injections; intraspinal* or *intrathecal injections; nasal injections; aural injections; rectal injections; urethral injections;* and *vaginal injections.*

Intradermal injections are injections between the layers of the skin. This method is used for administration of certain vaccines, but is most largely used for obtaining diagnostic reactions as in the case of sensitivity to proteins and in the administration of skin tests for specific immunity.

Hypodermic or **subcutaneous injections** are injections into the tissues under the skin and the volume injected is usually small. The injections are usually aqueous solutions.

Intramuscular injections are of fairly large volume and may include serums, solutions or suspensions of finely divided substances in aqueous or oily media.

Intravenous injections are intended to carry drugs directly into the blood stream. Serums, and solutions of chemicals, which must be free from solid particles, are administered in this manner.

Intraspinal or **intrathecal injections** in the form of serums, solutions of anesthetics or saline solutions are intended to carry these agents directly into the spinal canal.

The other types of injections referred to are for introduction into the particular body orifice indicated by means of syringes, spraying apparatus or by gravity.

Solutions for injection beneath the skin must be free from living micro-organisms, that is, *sterile,* in order to avoid serious consequences due to possible bacterial infections. It is also frequently necessary in the case of intravenous injections that the solution be isotonic with the blood stream (see p. 212).

ASEPSIS AND ANTISEPSIS

Asepsis is the word used to indicate the absence of disease germs. This condition is secured either by sterilization of the material or by the use of bactericides.

STERILIZATION

This important method of preserving medicinal substances and of rendering surgical appliances aseptic has now stepped from the confines of medicine into the field of pharmacy and the modern pharmacist must stand ready to prepare sterile products on demand. The call for aseptic dressings is now largely met by special manufacturers; so the prescriptionist is chiefly called upon to furnish sterile solutions.

Realizing this need, the U.S.P. XI contains a comprehensive monograph on sterilization that should be carefully read by all students. See U.S.P. XI, p. 466.

Summarized, the destruction or removal of bacteria or their spores and other living organisms, is usually accomplished by submitting the substance to the action of heated air or steam. Glass or metallic containers are best sterilized by heating at 170° C. for two hours in a hot air sterilizing oven or in an autoclave (Fig. 178) under steam pressure at a temperature of 115° C. maintained for not less than thirty minutes. "Flaming," or the application of a direct Bunsen burner flame to a surface for ten seconds may be used for sterilizing surfaces not adversely affected by such treatment. Medicinal solutions not injured by high temperatures are heated in a current of steam for one hour if the steam is at 100° C.; for thirty minutes if it is at 115° to 120° C. In the former case a steam sterilizer is used; in the latter case, an *autoclave* (Fig. 178) has to be employed.

Substances which are decomposed by heat above 100° C. and in which bacteria may multiply are usually sterilized by the fractional method using boiling water or streaming steam at 100° C. on three successive days for fifteen minute periods, keeping the container at 35° to 40° C. between the successive heatings.

If the solution (say, of alkaloids) is decomposed by the action of heat, approximate sterility may be attained by filtration through a porcelain (Berkefeld) filter, into containers which have been sterilized by steam, or by sterilizing all apparatus and containers employed in making and storing the solution and by dissolving the substance in sterilized distilled water (p. 414). If glycerin or oil is the solvent, it may be sterilized by heating for two hours at 120° to 130° C. in a dry air sterilizer.

In stoppering sterilized solutions, sterile rubber stoppers must be employed or nonabsorbent cotton stoppers wrapped in a layer of gauze and covered with stout paper or tin foil.

Cotton, bandages, gauzes, and other surgical dressings may be sterilized either by heating with steam at 115° C. in an autoclave or by dry heat at 160° to 170° C. in an oven. Such sterilized dressings must be kept aseptic by storing in sterile glass containers or by wrapping in sterilized parchment paper.

The monograph given in the National Formulary V outlines sterilization at low temperature or *pasteurization* (which means heating the material between 60° and 70° C. for one-half to one hour each day on six successive days) and sterilization by means of chemical agents (subjecting apparatus and material to the action of such antiseptics as alcohol, formaldehyde, phenol, etc.).

AMPULS

The preservation of sterile products in sealed glass tubes was first tried by Limousin in 1886 and since 1908, the practice has become very popular in medicine; so much so that the National Formulary VI lists 28 ampuls as compared with 7 in the former edition. A complete description of methods of filling and sterilizing ampuls is given in the Formulary. See pages 20 to 28.

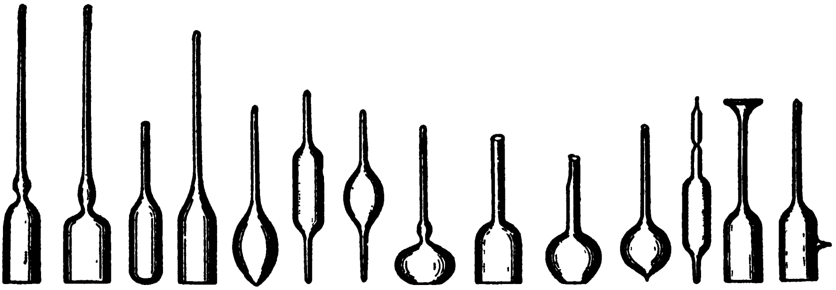

Fig. 273.—Various shapes of ampuls.

Ampuls are sealed glass tubes containing sterile medicaments for parenteral use. They may contain dry chemicals, solutions or suspensions in oil but most often they contain aqueous solutions. Ampuls of iodine are offered for topical application, wax ampuls of silver nitrate are prepared for instillation of the solution in the eyes of newborn babies and thin glass ampuls of amyl nitrite are offered for inhalation after crushing in a cloth.

The Ampul.—The glass tubes, usually purchased from special glass manufacturers, are made from a special type of glass known as No. 16 III, which is less alkaline than the average glass. Nitardy shows that satisfactory ampuls can be made from ordinary test tubes, but in passing it might be said that such ampuls are almost certain to contain enough free alkali to precipitate alkaloidal solutions. Ampuls are sometimes made with the open end flaring like a funnel, in order to facilitate filling (Fig. 273). Before filling, the ampuls must be cleansed and sterilized. Methods are described in the National Formulary VI, page 20. For the preparation of ampul solutions the Formulary provides *ampul water*

(p. 21) and *ampul oil* (p. 23). The water must correspond to tests for purity under "Redistilled Water, N.F." Ampul oil is any bland fixed oil corresponding to tests set forth.

Filling Ampuls.—Many filling devices, some very complicated and some quite simple, have been devised, the aim being to run the fluid down through the narrow neck as expeditiously as possible, a trick that is really not easy, since some provision should be made for exit of air as the fluid flows in. Some fill from a burette to the tip of which is attached a hypodermic needle; some use the modern type of large-sized graduated all-glass hypodermic syringe which can be easily sterilized; while the best appliance is one in which by a system of valves and air-tight containers the ampuls can be exhausted of air before the fluid is introduced into the container. Because of the partial vacuum in this container and in the ampuls found therein the fluid immediately fills the ampuls as soon as air is permitted to enter the apparatus.

Sealing the Ampul.—This is accomplished by bringing the tip of the filled and cleaned ampul into a small but hot flame of a blast lamp. This operation is not as simple as first appears, but, like everything else, practice will bring the knack. In large factories, for instance, such sealing is done by young girls.

Sterilization.—As mentioned above, the product in the ampul should reach the physician in a sterilized condition. Some ampuls contain chemical solutions which are self-sterilizing. Where sterilization is required for an official ampul, the National Formulary prescribes a method. The methods prescribed are listed as *Process A, B, C, D, E,* and *F.* Briefly summarized they may be described as follows:

Process A.—Direct flame (flaming). Bunsen burner.

Process B.—Dry heat. Oven at 160° to 190° C. for two hours.

Process C.—Steam under pressure. 110° to 130° C. in an autoclave.

Process D.—Moist heat at 100° C. (fractional sterilization, intermittent sterilization).

Process E.—Fractional sterilization at low temperature. Pasteurization.

Process F.—Filtration through sterile clay filter cone of Berkefeld or Chamberland type.

The National Formulary VI also provides tests for sterility of the finished ampuls with information as to what constitutes a proper sample.

ANTISEPTICS

An *antiseptic* is a substance that inhibits or stops the growth of or kills the bacteria but not the spores, out of which the bacteria develop; while a *disinfectant* or *germicide* kills not only the bacteria but also the spores. In modern language the three words are frequently used synonymously.

We have already learned (p. 987) that sterilization may be accomplished by use of chemical agents. These chemicals are of course antiseptics and throughout the foregoing pages of the book dozens of references are made to antiseptics. At this place a brief summary of antiseptics is all that is needed.

Antiseptics apparently act by destroying the vital processes of the protoplasm found in bacteria. A vast number of chemicals so act but their specific action varies according to the structure of the chemical, the nature of the solvent, the temperature and the physical condition of the infected matter. These several factors make the standardization

AMPULS OF THE NATIONAL FORMULARY

Latin name.	English name or synonym.	Ingredients (figures show amount used in 100 cc.).	Percentage of active ingredient.	Suggested method of sterilization.
Ampullæ aquæ redestillatæ.	Ampuls of triple-distilled water.			Process C.
Ampullæ bismuthi subsalicylatis.	Ampuls of bismuth salicylate.	10 Gm. of bismuth subsalicylate in ampul oil.	Not less than 57.6 and not more than 70 4 of the labeled amount in terms of bismuth oxide	Heating to 65° C. for 30 minutes.
Ampullæ caffeinæ cum sodii benzoate.	Ampuls of caffeine sodiobenzoate, N.F. V.	25 Gm. of caffeine with sodium benzoate in ampul water.	Not less than 45 and not more than 52 of the labeled amount in terms of anhydrous caffeine and not less than 48 and not more than 55 of the labeled amount in terms of sodium benzoate.	Process D.
Ampullæ calcii chloridi.	Ampuls of calcium chloride.	10 Gm. of calcium chloride in ampul water.	Not less than 95 and not more than 105 of the labeled amount.	Process C.
Ampullæ calcii gluconatis.	Ampuls of calcium gluconate.	10 Gm of calcium gluconate in physiological solution of sodium chloride.	Not less than 95 and not more than 105 of the labeled amount.	Process C.
Ampullæ camphoræ.	Ampuls of camphor in oil.	20 Gm. of camphor in ampul oil.	Not less than 93 and not more than 103 of the labeled amount.	Heating to 100° C. for 30 minutes.
Ampullæ dextrosi.	Ampuls of glucose.	50 Gm. of dextrose in ampul water.	Not less than 86 and not more than 96 of the labeled amount in terms of anhydrous dextrose.	Process D.
Ampullæ dextrosi et sodii chloridi.	Ampuls of dextrose and sodium chloride.	About 25 Gm. of anhydrous dextrose and 15 Gm. of sodium chloride in ampul water.		Process D.
Ampullæ emetinæ hydrochloridi.	Ampuls of emetine hydrochloride.	6 Gm of emetine hydrochloride in ampul water.	Not less than 84 and not more than 92 of the labeled amount in terms of anhydrous emetine hydrochloride.	Process D.
Ampullæ ephedrinæ sulfatis.	Ampuls of ephedrine sulfate.	5 Gm. of ephedrine sulfate in ampul water.	Not less than 72 6 and not more than 80.2 of the labeled amount.	Process D.
Ampullæ epinephrinæ hydrochloridi.	Ampuls of epinephrine hydrochloride.	Sterile solution of epinephrine hydrochloride, U S P.	In any other concentration, not less than 95 and not more than 105 of the labeled amount.	Process F with carbon dioxide.
Ampullæ ferri et ammonii citratum viridum.	Ampuls of green iron and ammonium citrate	10 Gm. of green iron and ammonium citrates; 0 5 Gm. of quinine and urea	Not less than 14.5 and not more than 16 of the labeled amount in terms of iron.	Process E.

Ampullæ hydrargyri salicylatis.	Ampuls of mercuric salicylate.	10 Gm of mercuric salicylate, 0.5 Gm. of quinine and urea hydrochloride in ampul oil.	Not less than 51 and not more than 62 4 of the labeled amount in terms of mercury.	At temperature not exceeding 65° C.
Ampullæ hydrargyri succinimidi.	Ampuls of mercuric succinimide.	1 Gm of mercuric succinimide in ampul water.	Not less than 47 7 and not more than 52.8 of the labeled amount in terms of mercury.	Any method not exceeding 65° C.
Ampullæ iodi.	Iodine swabs.	3 5 Gm. of iodine; 2.5 Gm. of sodium iodide; 30 cc of distilled water; alcohol, sufficient quantity.	Not less than 95 and not more than 105 of the labeled amount of iodine.	None (self-sterilizing).
Ampullæ magnesii sulfatis.	Ampuls of magnesium sulfate	50 Gm of magnesium sulfate in ampul water.	Not less than 95 and not more than 105 of labeled amount.	Process C.
Ampullæ methenaminæ.	Ampuls of methenamine.	40 Gm of methenamine in ampul water	Not less than 95 and not more than 105 of labeled amount.	Heating to 100° C. for 30 minutes.
Ampullæ pituitarii posterioris.	Ampuls of posterior pituitary.	Sterile solution of posterior pituitary, U S P		Process F.
Ampullæ procainæ hydrochloridi.	Ampuls of procaine hydrochloride.	Sterile solution of procaine hydrochloride, N.F.	In any other concentration, not less than 95 and not more than 105 of labeled amount.	Process D.
Ampullæ quininæ dihydrochloridi.	Ampuls of quinine dihydrochloride.	50 Gm. of quinine dihydrochloride in ampul water	Not less than 95 and not more than 105 of the labeled amount	Heating to 100° C. for 30 minutes.
Ampullæ quininæ et ureæ hydrochloridi.	Ampuls of quinine and urea hydrochloride	50 Gm of quinine and urea hydrochloride in ampul water	Not less than 54 8 and not more than 63 7 of the labeled amount in terms of anhydrous quinine.	Process E.
Ampullæ quininæ hydrochloridi et æthylis carbamatis.	Ampuls of quinine hydrochloride and urethane.	13 Gm of quinine hydrochloride with 6 5 Gm. of ethyl carbamate in ampul water	Not less than 92 5 and not more than 107 5 of the labeled amount.	Process E.
Ampullæ sodii cacodylatis.	Ampuls of sodium cacodylate.	30 Gm of sodium cacodylate in ampul water.	Not less than 69 and not more than 76 of the labeled amount in terms of anhydrous sodium cacodylate	Process C at 15 pounds' pressure for 20 minutes.
Ampullæ sodii chloridi.	Ampuls of sodium chloride	21.25 Gm. of sodium chloride in ampul water	Not less than 95 and not more than 105 of the labeled amount	Process C.
Ampullæ sodii citratis.	Ampuls of sodium citrate	2 5 Gm. of sodium citrate in ampul water	Not less than 95 and not more than 105 of the labeled amount.	Process C
Ampullæ sodii iodidi.	Ampuls of sodium iodide.	10 Gm of sodium iodide in ampul water	Not less than 92 and not more than 105 of the labeled amount	Process C.
Ampullæ sodii salicylatis.	Ampuls of sodium salicylate	20 Gm of sodium salicylate in ampul water	Not less than 93 and not more than 103 of the labeled amount	Heating to 100° C. for 30 minutes
Ampullæ sodii thiosulfatis.	Ampuls of sodium hyposulfite.	10 Gm of sodium thiosulfate in freshly boiled ampul water.	Not less than 60 5 and not more than 66 9 of the labeled amount in terms of anhydrous sodium thiosulfate.	Heating to 100° C. for 30 minutes.

of antiseptics, the comparison of antiseptic value, far from easy; they explain discrepancies in tables of antiseptic value; they account for the several methods of standardization of antiseptics found in medical literature.

In 1928, the Food, Drug and Insecticide Administration of the U. S. Department of Agriculture promulgated a rule which was understood as meaning that a commercial "antiseptic" had to be a "germicide." This ruling caused much controversy and it was later modified to imply that a medicinal preparation intended for germ conditions could be labeled and sold as an "antiseptic" even though possessing only inhibitory power and incapable of germicidal action in the sense of germ destruction, provided the preparation was not claimed by the manufacturer to possess germicidal action. In the words of a court decision "To say that a substance is 'antiseptic' is merely to affirm that it has a tendency to prevent putrefaction, decay or the development or increase of bacteria and not to affirm any particular potency."

Of the several methods of standardization, the one most largely used in this country is the Anderson and McClintic modification of the Rideal-Walker method of establishing the *phenol coefficient.* For details the reader is referred to Reprint No. 675 of the U. S. Health Reports. Here it can only be stated that the test consists of comparison of the antiseptic action of phenol solutions of known strength and of the disinfectant under examination upon *Bacillus typhosus.*

The series tested should include dilutions strong enough to kill *B. typhosus* in five minutes and others weak enough to fail to do so in fifteen minutes. The dilutions are placed in test tubes and are heated on a water bath at 20° C. and are then inoculated with a broth culture of *B. typhosus* at fifteen-second intervals. Cultures are then prepared from these inoculations and those in which bacterial growth is observed are recorded as positive. To obtain the coefficient, the weakest dilution of the unknown antiseptic that kills in five minutes is divided by the weakest dilution of phenol that kills in the same time. The same is done for the lowest strength that kills in ten minutes and in fifteen minutes. The three quotients are then added and then divided by three, this final quotient being chosen as the phenol coefficient.

DISINFECTION

Disinfection is the application of antiseptics to polluted matter, notably bodily excretions, or to the contaminated air of the sick room. This latter phase must be given brief mention since the pharmacist furnishes disinfectants to his customers. These disinfectants may be various antiseptic solutions or may be the material for producing gaseous disinfection or *fumigation.* For the latter purpose ozonizing apparatus (p. 413), sulfur candles (for producing SO_2) and formaldehyde disinfecting apparatus are now most largely used; formaldehyde being the favorite. In formaldehyde the gas is either produced by the incomplete combustion of wood alcohol in special lamps (p. 649) or by use of candles made of paraformaldehyde or else Formaldehyde Solution, U.S.P. is mixed in a pail with lime or with potassium permanganate, when copious fumes of HCHO are evolved.

Many health boards are now dropping fumigation, claiming that disinfection is satisfactorily accomplished by a thorough airing of the room.

BIBLIOGRAPHY

Bacteria.—(History) See Magnin-Sternberg and Hiss-Zinsser (this book, p. 971). (General Properties) Marpmann, Ph. Jl., III, 12, 1881, 89, 157 and 184; Hatch, *ibid.*, III, 22, 1891, 271, 289 and 330; Woodhead, *ibid.*, III, 23, 1892, 319 and 334; Kanthack, A.Ph.A., 42, 1894, 882.

Immunity.—Hektoen, Pract. Dr., 47, May, 1929, 24.

Antidiphtheric Serum.—Behring and Kitasato, Ph. Jl., III, 31, 1890, 557; Behring, Ber. dtsch. Pharm. Ges., 3, 1893, 279; McClintock, A.Ph.A., 44, 1896, 254; Hewlett, Ph. Jl., 73, 1904, 377; Crawford and Foster, A.J.P., 90, 1918, 765; Ruppel, Ber. dtsch. Pharm. Ges., 30, 1920, 328.

Vaccine Virus.—Stewart, Jl. A.Ph.A., 4, 1915, 1446.

Antitoxins and Vaccines.—Yarbrough, West. Dr., 32, 1910, 121; Diner, Jl. A.Ph.A., 3, 1914, 177; McCoy, Jl. A.Ph.A., 9, 1920, 573.

Intravenous Medication.—See bibliography, under *arseno-organics* and arsphenamine on p. 788.

Sterilization.—Cook, Dr. Circ., 54, 1910, 161; Lesure, Am. Dr., 58, 1911, 346; Virden, Dr. Circ., 60, 1916, 212; Anon., Pract. Dr., 37, Dec., 1919, 37; Dezeine, Pharm. Era, 53, 1920, 334; Linton, Jl. A.Ph.A., 9, 1920, 589; Roy, Jl. Soc. Ch. Ind., 44, 1925, 611B; Rapp, A.J.P., 101, 1929, 839; Bauer, Dr. Circ., 74, Aug., 1930, 48; Perrins, Ph. Jl., 124, 1930, 666; Deussen, Arch. Pharm., 268, 1930, 190; Schwenke, Ph. Zt., 76, 1931, 439; Burn and co-workers, Ph. Jl., 127, 1931, 8; Muntsch, *ibid.*, 127, 1931, 317; Thomann, *ibid.*, 128, 1932, 310; Back, *ibid.*, 128, 1932, 307 and 370; Himwicke, *ibid.*, 128, 1932, 350; Davis, *ibid.*, 129, 1932, 130 and 133, 1934, 68; Coulthard, *ibid.*, 130, 1933, 266.

Ampuls.—Limousin, Am. Dr., 15, 1886, 216; Mayo, A.Ph.A., 57, 1919, 1106; Nitardy, Jl. A.Ph.A., 2, 1913, 319; Lascoff, *ibid.*, 3, 1914, 689; E'we, Jl. Frank. Inst., 189, 1920, 649; Dann, Ph. Zt., 70, 1925, 1522; Rapp, *ibid.*, 74, 1929, 464; Eleizegui, C.A., 24, 1930, 5953; Lucas, Ph. Jl., 129, 1932, 9; Pritchard, *ibid.*, 129, 1932, 350.

Antiseptics.—Bucholz, A.Ph.A., 26, 1878, 443; Smith, Am. Dr., 57, 1910, 100; Gilmour, A.Ph.A., 58, 1910, 293; Martindale, Ph. Jl., 85, 1910, 668; Gawalowski, Merck's Rep., 20, 1911, 233; Hoffman and Evans, Jl. Ind. Eng. Ch., 3, 1912, 835; Cooper, C.A., 7, 1913, 2400 and Jl. Soc. Ch. Ind., 44, 1925, 334B; Maben and White, Ch. and Dr., 76, 1915, 144; "Chemicus," Ph. Jl., 95, 1915, 324; Norton and Hsu, C.A., 10, 1916, 1203; E'we, Taylor, Austin, Rettie and Cavel, Yearbook A.Ph.A., 7, 1918, 206 and 407; E'we, Proc. P.P.A., 45, 1920, 248; Beal and Perry, Jl. Ind. Eng. Ch., 12, 1920, 253; Joachimoglu and co-workers, Jl. Soc. Ch. Ind., 44, 1925, 334B; Reynolds, C.A., 19, 1925, 2103; Gjaldbaek, C.A., 23, 1929, 4298; Ed., Jl. A.Ph.A., 17, 1928, 629; Patterson, Am. J. Pub. Health, 22, 1932, 465.

Phenol Coefficient.—Rideal and Walker, Ch. and Dr., 63, 1903, 975; Anderson and McClintic, U. S. Health Reports, Reprint 675; Hale, C.A., 7, 1913, 3137; Myers and Thienes, Jl. A.M.A., 84, 1925, 1895; Harvey, A.J.P., 100, 1928, 524; Kingery and Adkisson, C.A., 23, 1929, 1989; Rose, A.J.P., 101, 1929, 52; Miller, *ibid.*, 103, 1931, 324; Allen and Wright, Ph. Jl., 126, 1931, 465; Malcolm, C.A., 26, 1932, 1956.

Fumigation.—Dixon, Jl. A.M.A., 63, 1914, 1025; Hamilton, Ph. Jl., 98, 1917, 453.

PART V

PHARMACEUTIC TESTING

CHAPTER LIII

INTRODUCTORY

On the foregoing pages enough has been said to emphasize the importance of examining pharmaceuticals and chemicals, both as to composition and also the quantity of each component. The subject of such testing is called *analytic chemistry,* a branch of science the many details of which are clearly beyond the scope of this work. In former editions of this book some three-score pages were devoted to this important subject. Since 1925, however, admirable books devoted entirely to the subject of pharmaceutical assaying have appeared (see List of Reference Books, pp. 15, 16), hence the subject can be considered at this place in mere outlines.

Analytic chemistry is divided into two subdivisions—*qualitative analysis,* which aims to find the constituents of a compound, and *quantitative analysis,* by means of which we can estimate the quantity of each ingredient. Quantitative analysis is, in turn, divided into a number of classes: such as gravimetric, volumetric, gasometric, and colorimetric analysis.

Gravimetric analysis is where the quantity of ingredient is determined by conversion into an insoluble compound containing a definite proportion of the ingredient, collecting and weighing the precipitate, and from the weight obtained estimating the amount of the ingredient by molecular proportions.

Volumetric analysis (or *titration*) is where the quantity of ingredient is determined from the amount of a definite standard solution of a chemical (*volumetric solution*) required to combine with it exactly; the amount of this volumetric solution required exactly to complete the reaction is usually denoted by the change in color produced by a third chemical, called an *indicator.*

Assaying is a term applied in pharmacy to the quantitative estimation of the active ingredient of a mixed product, notably a drug. As the quantity is sometimes estimated by gravimetric analysis and sometimes by volumetric analysis, the process is merely a modification of these, the only difference being that some process of extraction must first be employed.

The *apparatus* used in pharmaceutic testing have been referred to in the chapters comprising Part I. For qualitative analysis, funnels, beakers, spritz bottles, flasks, evaporating dishes, filter paper, and Bunsen burners are required, and these have already been described. In addition thereto it is necessary to have test tubes and test tube racks (p. 166); red and blue litmus paper (which is filter paper dipped in a decoction of the lichen, litmus, and treated with acid to make it red, or alkali to make it blue); blue glass; and platinum wire and foil.

The chemical to be analyzed is usually made into a solution and treated with solutions of other chemicals. Such solutions are called *test solutions.* This phrase is frequently abbreviated to T.S. (example, potassium iodide T.S.).

The test solutions are usually prepared by making a 10 to 20 per cent solution of the chemical (called *reagent*) in distilled water, but many of the test solutions must be prepared by special treatment. The strength of test solutions usually approximates 10 per cent, but in U.S.P. XI, the strength of most of them is based upon normality (p. 1004). A recipe for each test solution directed by the Pharmacopœia is found in the appendix to that standard (pp. 548–557), to which the reader is referred.

These test solutions should be kept in special bottles, closed either with glass or rubber stoppers. Such a test solution bottle is shown in Fig. 274.

While most qualitative analyses are performed with test solutions, the reagent, hydrogen sulfide, is employed as a gas and is usually generated by action of sulfuric acid on ferrous sulfide in a Kipp's generator (Fig. 275), which acts automatically. Then sometimes the reagent is employed in solid form. Thus, borax is fused for the borax bead test, sodium carbonate and potassium nitrate are melted on platinum foil in several of the fusion tests, etc.

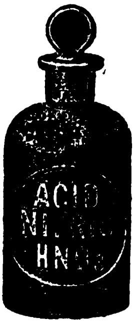

Fig. 274.—Reagent bottle.

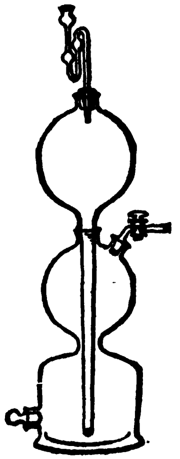

Fig. 275 —Kipp's gas generator.

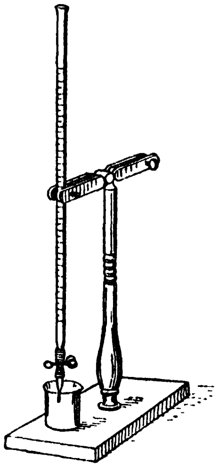

Fig. 276.—Burette and holder.

In quantitative analysis the apparatus used are crucibles, desiccators, analytic balances, measuring vessels, such as burettes (Fig. 276), pipettes, measuring cylinders, 100-cc. and 1000-cc. bottles. The reagents used are practically the same as in qualitative analysis, with the additional line of volumetric solutions, the manufacture of which will be discussed a few pages farther on.

In drug assays the apparatus is practically the same as that just mentioned, but in addition thereto, since the active principle is usually extracted by shaking out of the watery solution with ether or chloroform (separation from an immiscible solvent), a separatory funnel is required.

The detection of the ingredients of a compound in qualitative analysis is accomplished in several ways:

I. *By production of a characteristic precipitate:* thus a solution of a sulfate when mixed with barium chloride T.S. gives a white precipitate, insoluble in boiling nitric acid.

II. *By production of a characteristic color in a solution:* thus a diluted solution of copper sulfate gives a deep azure blue solution with excess of ammonia water.

III. *By production of a characteristic odor:* thus an acetate warmed with alcohol and sulfuric acid gives the pleasant odor of acetic ether.

IV. *By transmitting a characteristic color to a colorless Bunsen flame:* thus a trace of sodium salt on a loop of platinum wire placed in a colorless Bunsen flame makes it a vivid yellow.

V. *By giving a characteristic color to a borax bead:* thus if borax is fused on a loop of platinum wire and a trace of a manganese salt added to the bead, which is then fused once more, the cooled solidified bead will be found to possess a beautiful amethyst color.

VI. *By giving a characteristic color to specially prepared test paper:* thus borax gives buff-colored turmeric paper a red-brown tint.

VII. *By producing a play of colors when brought in contact with the reagent on a porcelain surface:* thus most alkaloids give characteristic color reactions when treated with a drop of sulfuric acid and a trace of potassium dichromate.

VIII. *By leaving a characteristic residue on heating on charcoal with a blowpipe:* thus zinc salts when treated with cobaltous nitrate and heated with a blowpipe leave a vivid green spot.

CHAPTER LIV

QUALITATIVE INORGANIC TESTS

ON pages 448 to 454 of U.S.P. XI are found a summary of the tests for metallic ions and for acid ions. For pharmacopœial applications of these tests see Parts III and IV of this book.

Free chlorine liberates iodine from potassium iodide.

Hydrochloric acid and **chlorides** give, with silver nitrate T.S., a white curdy precipitate insoluble in nitric acid, but soluble in ammonia water. This precipitate is silver chloride (AgCl).

Hypochlorites, when treated with an acid, evolve odor of chlorine.

Chlorates, on heating with hydrochloric acid, evolve chlorine. On heating strongly, chlorates evolve oxygen.

Free bromine liberates iodine from potassium iodide. (See chlorine test for hydrochloric acid, in U.S.P., p. 21.)

Hydrobromic acid and **bromides** give, with silver nitrate T.S., a yellowish-white precipitate insoluble in diluted nitric acid, but soluble in ammonia water. This precipitate is silver bromide (AgBr). Bromides plus chlorine water liberate bromine which dissolves in chloroform producing a yellow solution.

Bromic acid and **bromates** liberate bromine (which colors chloroform brown yellow) when treated with strong acids or other chemicals.

Free iodine gives deep blue color to starch mucilage, which color is discharged on addition of sodium thiosulfate solution. It also transmits to chloroform a violet color.

Hydriodic Acid and Iodides.—Chlorine water or ferric chloride liberates free iodine which gives violet color to chloroform. Silver nitrate gives yellow precipitate, insoluble in ammonia water as well as in nitric acid. This precipitate is silver iodide (AgI).

Iodic Acid and Iodates.—Iodine is liberated by action of acids and other chemicals, transmitting a yellowish-brown color to solution.

Hydrofluoric acid and **fluorides** give off vapors which etch glass. (Fluorides must be warmed with sulfuric acid.)

Sulfides, when treated with a diluted acid, give off hydrogen sulfide gas, characterized by its bad smell and its ability to blacken paper moistened with lead acetate T.S.

Sulfurous acid and **sulfites** when heated (the sulfites when treated with a diluted acid) give off sulfur dioxide gas, characterized by its suffocating odor and its ability to blacken paper moistened with mercurous nitrate T.S. When treated with zinc and hydrochloric acid, they evolve hydrogen sulfide gas and they decolorize iodine and permanganate solutions.

Sulfuric Acid and Sulfates.—Barium chloride T.S. gives a white precipitate, insoluble in hydrochloric acid. This precipitate is barium sulfate ($BaSO_4$).

Thiosulfates, on treatment with a strong acid, liberate sulfur dioxide, while sulfur precipitates from the solution.

Nitrous acid and **nitrites** liberate iodine from potassium iodide with evolution of N_2O_4 gas; decolorize potassium, permanganate when in acid solution, and are reduced to ammonia when treated with a metal and an acid.

Nitric Acid and Nitrates.—The free acid discharges the color of indigo solution and colors wool yellow. The acid or a nitrate, plus sulfuric acid, converts green ferrous sulfate to red-brown ferric sulfate. If only a small quantity is used and the solutions "layered," a black-brown ring is shown at point of contact of the two liquids.

Boric acid gives the alcohol flame a green tinge.

Borates give similar flame when treated with a few drops of concentrated sulfuric acid and a little alcohol and then ignited.

Hypophosphites act as reducing agents; that is, when in acid solution or when heated with solutions of salts of silver, copper, and mercury, the metal is eventually precipitated. On heating, hypophosphites yield spontaneously combustible gas, phosphine (PH_3). (See p. 474.)

Phosphorous acid reduces solution of silver nitrate and mercuric chloride as do hypophosphites. It also gives a white precipitate with barium chloride T.S.

Phosphoric acid and **phosphates** give white, crystalline precipitate with magnesium mixture,[1] a yellow precipitate, soluble in ammonia and nitric acid with silver nitrate T.S., a yellow precipitate on warming with ammonium molybdate T.S. The acid differs from metaphosphoric acid in coagulating albumin; from hypophosphorous acid in giving a yellow precipitate with silver nitrate.

Metaphosphoric Acid.—(See p. 453.)

Pyrophosphoric acid and **pyrophosphates** give a white precipitate with silver nitrate whereas phosphates turn yellow. They also usually precipitate ferric salts.

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[1] *Magnesia Mixture T.S.*—Dissolve 5.5 Gm. magnesium chloride, and 7 Gm. ammonium chloride in 65 cc. distilled water; add 35 cc. ammonia water, U.S.P.; set aside a few days in a well-stoppered vessel and then filter.

Carbonic acid and **carbonates** effervesce on addition of a diluted acid. They give white precipitates with lime water.

Silicates.—Soluble silicates (those of the alkaline metals), when treated with sulfuric acid, give a gelatinous precipitate of silicic acid, $Si(OH)_4$. Soluble silicates can be precipitated from aqueous solution by addition of alcohol.

Permanganates give rose-colored aqueous solution and the color is discharged on addition of oxidizable substances.

ORGANIC ACIDS

Acetic acid and **acetates,** when warmed with alcohol and sulfuric acid, give off odor of acetic ether. Neutral acetates give deep red color with ferric chloride.

Oxalic acid and **oxalates** give white precipitate of calcium oxalate on treatment with the solution of a calcium salt. They also give a white precipitate with barium chloride, soluble in nitric acid.

Lactates give the odor of acetaldehyde when heated with unacidulated solution of potassium permanganate.

Tartaric acid and **tartrates** give white, crystalline precipitate of cream of tartar with addition of the proper quantity of potassium salt. When gently warmed with an ammoniacal solution of silver nitrate, the latter is reduced, and a silver mirror forms.

Citric acid and **citrates,** when boiled with calcium solutions deposit white granular precipitate of calcium citrate.

Cyanides give a white precipitate with silver nitrate T.S., soluble in excess of cyanide solution. When treated with ferrous and ferric salts, alkali, and then an excess of acid, a blue color (ferric ferrocyanide) is produced.

Ferrocyanides give deep blue precipitate with ferric salts.

Ferricyanides give deep blue precipitate with ferrous salts.

Benzoates give flesh-colored precipitates with ferric salts.

Salicylates give violet color, or precipitate with ferric salts. When warmed with concentrated sulfuric acid and methyl alcohol, it gives the odor of methyl salicylate (oil of wintergreen).

Gallic acid and **gallates** give, with ferric chloride T.S., a blue-black color.

Tannic acid and **tannates** give, with ferric chloride T.S., a blue-black precipitate. The acid differs from gallic acid yielding precipitates with solutions of alkaloids, glucosides, gelatin, albumin, and starch.

THE METALS

Potassium and **its salts** give a violet tint to a colorless flame. When the proper quantity of tartaric acid or sodium bitartrate is added, a white crystalline precipitate (cream of tartar) results. When treated with platinic chloride T.S., a yellow, crystalline precipitate of potassio-platinic chloride is formed. When treated with sodio-cobaltic nitrite solution, a yellow precipitate falls.

Sodium and **its salts** give a brilliant yellow tint to a colorless flame.

Lithium and **its salts** give crimson color to a nonluminous flame.

Ammonium salts, when heated with other alkalis, give off ammonia gas.

Magnesium salts give, with sodium phosphate, in the presence of ammonium chloride and ammonia water, a white, crystalline precipitate.

Calcium compounds give, with ammonium oxalate, a white precipitate, insoluble in acetic acid, but soluble in hydrochloric acid.

Strontium compounds give a crimson flame. Diluted sulfuric acid and solutions of sulfates give a white precipitate of strontium sulfate, which is soluble in strong acids.

Barium salts give a green flame. With potassium dichromate T.S. they give a yellow precipitate of barium chromate. With sulfuric acid they give a white precipitate of barium sulfate, insoluble in boiling nitric acid.

Zinc salts give, with hydrogen sulfide T.S. or with ammonium sulfide T.S., a white precipitate of zinc sulfide; with potassium ferrocyanide T.S., a white gelatinous precipitate of zinc ferrocyanide. Heated with blowpipe with cobaltous nitrate T.S. it turns a vivid green.

Manganese preparations, fused with alkaline hydroxides or carbonates and an oxidizing agent (potassium nitrate or chlorate), give a green mass (alkaline manganate), and this, when boiled with water, gives a purple solution (of alkaline permanganate). Solutions of manganous salts give, with ammonium sulfide T.S., a flesh-colored precipitate of manganese sulfide.

Aluminum salts give, with ammonia water, a white, gelatinous precipitate of aluminum hydroxide, insoluble in excess of ammonia water; with potassa or soda they give the same precipitate, but it is soluble in excess of potassa or soda.

Ferrous salts give, with potassium ferricyanide, a blue color or precipitate.

Ferric salts give a red-brown precipitate of ferric hydroxide with ammonia or soda or potassa. With potassium ferrocyanide they give a deep blue color or precipitate, and with potassium thiocyanate, a blood-red color.

Arsenic and **its compounds** give, with hydrogen sulfide, a bright yellow precipitate of arsenic sulfide, which is soluble in ammonium carbonate T.S. and in ammonium sulfide T.S. With ammoniacal solution of copper sulfate[1] they give a green precipitate, while acid solutions dropped on a sheet of metallic copper coats the metal with a gray film of metallic arsenic. See also Marsh's Test (p. 580), Bettendorf's Test (p. 580 and below), and Gutzeit's Test (p. 580).

Antimony and **its compounds** give, in acid solution with hydrogen sulfide, an orange precipitate of antimony sulfide, soluble in ammonium sulfide T.S.

Cadmium and **its compounds** give, in acid solution with hydrogen sulfide, a yellow precipitate, insoluble in ammonium sulfide T.S.

Copper salts give, with potassium ferrocyanide T.S., a red-brown precipitate of copper ferrocyanide. With ammonia water they give a blue-white precipitate of cupric hydroxide, which, when treated with excess of ammonia water, dissolves to an azure-blue liquid (see Cupric Ammonium Sulfate T.S., below). If a bright piece of steel is dipped into a copper solution, it becomes coated with metallic copper.

Bismuth salts in concentrated nitric or hydrochloric acid solution yield, when poured into large amount of water, a white precipitate (of the "sub" salt of bismuth). With hydrogen sulfide, solutions of bismuth salts give a black precipitate of bismuth sulfide.

Lead salts give, with hydrochloric acid, a white precipitate of lead chloride, which is sparingly soluble in water; with diluted sulfuric acid it gives a white precipitate of lead sulfate; with hydrogen sulfide, or alkaline sulfides, a black precipitate of lead sulfide; with potassium iodide, a yellow precipitate of lead iodide.

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[1] **Cupric Ammonium Sulfate Test Solution.**—To copper sulfate T.S. add ammonia water, drop by drop, until the precipitate at first formed is nearly, but not completely redissolved, then filter. This solution should be freshly made when required.

Mercury salts (both "ous" and "ic") give, with hydrogen sulfide, a black precipitate of mercuric sulfide.

Mercurous salts give, with hydrochloric acid, a white precipitate of mercurous chloride.

Mercuric salts give no precipitate with hydrochloric acid. They give with ammonia a white precipitate (ammoniated mercury); with potassium iodide, a red precipitate of mercuric iodide, soluble in excess, and with sodium hydroxide, a yellow precipitate of mercuric oxide.

Silver salts give, with hydrochloric acid, a curdy white precipitate of silver chloride, soluble in ammonia water, but insoluble in nitric acid.

Group Impurities.—Aside from the tests for specific impurities given on the foregoing pages, the Pharmacopœia in several cases directs tests for groups of impurities, such as *heavy metals, excess of alkali* and *nonvolatile impurities.* For these, consult U.S.P. XI.

TURBIDIMETRIC TESTS

In previous editions of the Pharmacopœia there have been a number of tests directing that addition of certain reagents to certain official chemicals should not produce "more than a faint turbidity" or "more than an opalescence." Such vague wording led to a number of trade controversies and even litigation, so in U.S.P. XI these tests have been placed upon a definite scientific basis, a special chapter being given in Part II on "Turbidimetric Tests."

Condensing these tests it may be stated that a dilute solution of the chemical is placed in a glass cylinder and the turbidity produced upon adding a specified quantity of the reagent is matched against a standard dilution of the impurity sought when placed in a similar cylinder and treated with the same quantity of reagent.

The *impurities sought* in the turbidimetric tests of U.S.P. XI are *chloride* and *sulfate,* a definite prescribed quantity of the official chemical (usually 1 or 2 Gm.) is dissolved in 30 or 40 cc. of water the specified amount of reagent or reagents are added and the mixture diluted to 50 cc. The matching fluid is a definite prescribed dilution of *n*/50 silver nitrate for chloride or of *n*/50 sulfuric acid for sulfate. The Pharmacopœia also provides similar *lead* tests for citric and tartaric acids and also for potassium bitartrate.

SYSTEMATIC CHEMICAL ANALYSIS

The pharmacopœial tests given on preceding pages, while important and valuable, give us information that is somewhat disjointed.

If we suspect that a liquid contains zinc, we may try the tests for zinc given on p. 534, but suppose the liquid contains magnesium and iron as well as zinc, how would we then proceed? Or suppose we had no idea what metals the solution contains, how would we begin?

In analytic chemistry, as in everything else in science, system is the secret of success, and it is to systematic analysis to which we now must refer. This is performed by separating the several elements in a solution into groups by the use of certain chemicals which we call "group reagents." The important group reagents are:

First, hydrochloric acid (HCl); second, hydrogen sulfide (H_2S); third, ammonium sulfide (NH_4HS); fourth, ammonium carbonate, $(NH_4)_2CO_3$; applying them one after another to the solution under examination.

Now, suppose we have a solution containing *all* the elements used in pharmacy, we would take the solution and add.

Hydrochloric acid, when there would be precipitated out Hg (ous), Pb, and Ag as insoluble chlorides. The liquid is separated from the precipitate by filtration, and through the filtrate we would pass:

Hydrogen sulfide (*gas*), when we would get a precipitate of: (*a*) Cd, Cu, Hg (ic), Pb, Bi. (*b*) As, Sb, and Sn as insoluble sulfides. The precipitate can be separated into groups "a" and "b" by digestion in NH_4HS, in which group "b" dissolves, leaving group "a" behind. In the meanwhile the filtrate from the H_2S precipitate is treated with NH_4Cl, NH_4OH, and

Ammonium sulfide, which precipitates from it (*a*) Fe, *Al*, *Cr;* (*b*) *Zn*, Mn, Co, and Ni. All save those in italics as sulfides. The italicized as hydroxides.

Group "a" of this precipitate, when dissolved in hydrochloric and nitric acid, is precipitated by ammonia water. Group "b," under same treatment, is not. By this method the two groups are separated. The filtrate from the NH_4HS precipitate is now treated with

Ammonium carbonate, when down comes Ba, Sr, and Ca, as insoluble carbonates. To the filtrate from this precipitate is added

Ammonium phosphate, when there is precipitated Mg as phosphate. The filtrate will now hold only Li, Na, K, and NH_4, and this is considered the last group.

By this method we have separated the metals into seven groups, as follows:

I.	Li	K	Na	NH_4
II.	Mg	Ca	Sr	Ba
III.	Zn	Mn	Co	Ni
IV.	Al	Fe	and	Cr
V.	As	Sb	Sn	
VI.	Cd	Cu	Hg	(ic) Bi
VII.	Hg	(ous)	Pb	and Ag.

Only the symbols are given above, as it is expected that the preceding chapters of this book have been read and mastered.

Some books on analytic chemistry number these groups differently, beginning with Hg (ous) and Ag as the first group, but this is of small importance, the main point being the separation of the 24 metals into seven simple groups, from which, in turn, the metals themselves can be separated without great difficulty. How this separation of the small groups is carried on is beyond the scope of this book, and the reader is referred to one of the books on analytic chemistry mentioned in Preface.

A summary of the more important individual tests may be useful.

The following metals give characteristic color with *borax bead:*

Manganese	Amethyst.
Cobalt	Blue.
Copper	Green.
Iron	Red.

The following flame tests are characteristic:

Strontium (also lithium)	Crimson.
Calcium	Red-yellow.
Copper	Blue-green.
Potassium	Violet.
Sodium	Yellow.
Boric acid plus alcohol	Green.

The following hydrogen sulfide precipitates are characteristic:

White	Zinc (from alkaline solution).
Flesh color	Manganese (from alkaline solution).
Yellow	Arsenic and tin (from acid solution).
Orange	Antimony (from acid solution).
Blacks	Mercury, copper, lead (from acid solution).

The other elements will not precipitate with H_2S.

The following special tests are characteristic:

SUBSTANCE	REAGENT	REACTION
Acids and Their Salts.		
H_2SO_4.	Barium chloride.	White precipitate.
HCl.	Silver nitrate.	White precipitate.
HBr.	Silver nitrate.	Yellow precipitate.
Phosphoric acid.	Magnesium sulfate.	White crystalline precipitate.
Carbonic acid.	Lime water.	White precipitate.
Nitric acid.	Green $FeSO_4$ solution.	Changed to *red* or *black* $Fe_2(SO_4)_3$ solution.
Thiosulfuric acid.	Sulfuric acid.	Vapors of SO_2 and precipitate of sulfur.
Sulfurous acid.	Sulfuric acid.	Vapors of SO_2.
Tartaric acid.	Ammoniacal silver nitrate.	Mirror of metallic silver.
Acetic acid.	H_2SO_4 and alcohol.	Odor of acetic ether.
Metallic Salts.		
Zinc.	Hydrogen sulfide.	White precipitate.
Calcium.	Ammonium oxalate.	White precipitate.
Magnesium.	Sodium phosphate.	White precipitate.
Iron (ic).	Potassium ferrocyanide.	Blue precipitate.
Iron (ous).	Potassium ferricyanide.	Blue precipitate.
Silver.	Sodium chloride.	White precipitate.
Aluminum.	Solution of soda.	White gelatinous precipitate.
Lead	Potassium chromate.	Yellow precipitate.
Arsenic. Antimony.	Test by Marsh's, Fleitmann's, or Gutzeit's test, as explained on p. 1000.	

Tests for organic chemicals are too numerous and varied to admit of a tabulated statement; hence the reader is referred to the pharmacopœial tests for such substances, found scattered through Part IV.

CHAPTER LV

QUANTITATIVE ANALYSIS

As mentioned on page 995, we are able to examine chemicals not merely as to ingredients, but also can ascertain the quantity of each ingredient. The latter work is the object of quantitative analysis. The three methods of quantitative analysis usually employed are volumetric analysis, gravimetric analysis, and gasometric analysis.

VOLUMETRIC ANALYSIS

Volumetric analysis is the most largely employed process of quantitative analysis as far as pharmacy is concerned; the Pharmacopœia directing this method in the estimation of the strength of drugs whenever possible. The volumetric processes of the Pharmacopœia, with but two exceptions (the use of Fehling's solution and the use of Koppeschaar's solution, page 1026), fall into four groups:

I. Acidimetry or alkalimetry.

II. The use of iodine volumetric solution or its complement, sodium thiosulfate volumetric solution.

III. Oxidation with potassium permanganate volumetric solution or with potassium dichromate volumetric solution.

IV. The use of silver nitrate volumetric solution or its complements, potassium thiocyanate volumetric solution and sodium chloride volumetric solution.

Before discussing these several groups of volumetric analysis it is advisable to quote what the Pharmacopœia says about volumetric solutions, with special emphasis laid on the explanation of *normal solutions, decinormal solutions*, and *centinormal solutions*.

The eleventh revision of the Pharmacopœia (Part II, page 561) gives explicit general directions as accuracy in volumetric work and these directions should be carefully read by all students. It then proceeds to discuss volumetric solutions as outlined below.

Normal $\left(\frac{N}{1}\right)$ *volumetric solutions* according to the Pharmacopœia are "those which contain in 1000 cc., in any stated reaction, the chemical equivalent of 1.0078 Gm. of hydrogen." It then proceeds to state that a normal solution of a univalent reagent contains in 1 liter, the molecular weight of that reagent expressed in Gm.; that of a bivalent reagent one half of the molecular weight expressed in Gm.; if trivalent, one third of the molecular weight expressed in Gm. The examples cited are: hydrochloric acid, HCl, has the molecular weight 36.47; therefore 1 liter of normal solution should contain 36.47 Gm. absolute HCl. Sulfuric acid, H_2SO_4, has the molecular weight, 98.08; hence 1 liter of normal solution will contain 98.08 ÷ 2 or 49.040 Gm. absolute H_2SO_4.

Potassium hydroxide KOH, has the molecular weight, 56.10; hence 1 liter of normal solution will contain 56.10 Gm. absolute KOH.

Potassium dichromate has the molecular weight, 294.21 and liberates 3 atoms of oxygen. One molecule of it is therefore equal to 6 atoms of hydrogen and 1 liter of its normal solution should therefore contain 294.21 ÷ 6 or 49.035 Gm. absolute dichromate.

The monograph further explains why 1 liter of tenth-normal potassium permanganate contains 3.1606 Gm. absolute permanganate (see this book, p. 1015) and points out that a tenth-normal, in hundredth-normal, in fiftieth-normal, in double-normal and in half-normal volumetric solutions contain respectively one tenth, one one hundredth, one fiftieth, twice and half the amount of reagent found in the normal solution. It further gives the two styles of abbreviations used for these strengths of volumetric solutions:

Tenth-normal $\frac{N}{10}$ or 0.1 *n*.

Hundredth-normal $\frac{N}{100}$ or 0.01 *n*.

Fiftieth-normal $\frac{N}{50}$ or 0.02 *n*.

Double-normal $\frac{2N}{1}$ or 2 *n*.

Half-normal $\frac{N}{2}$ or 0.5 *n*.

Lastly it discusses empiric solutions, those not adjusted upon a molecular basis, but which are usable since their exact strengths are known and the proper factor necessary in calculations can be determined. All of these details should be carefully read in the Pharmacopœia (pp. 561 to 563) by the student.

In preparing these volumetric solutions, the dried chemical is weighed on an accurate balance (p. 50) and is dissolved in distilled water in a standardized liter flask (p. 57). Other apparatus needed in volumetric analysis are pipettes (p. 57), burettes (p. 57) and chemical flasks of various sizes.

Acidimetry and Alkalimetry.—This group includes the estimation of alkalis by use of a volumetric solution of an acid or the estimation of acids by the use of a volumetric solution of an alkali. The process can be best illustrated by a typical example. Taking the pharmacopœial determination of sodium hydroxide, for instance, we find (p. 1010) that it is accomplished by use of normal volumetric solution of sulfuric acid, and the theory of this kind of estimation is that sufficient of the acid solution is added to make the product exactly neutral—to make pure sodium sulfate. To know when this neutrality is reached, we use some substance which by change of color will show whether the liquid is acid or alkaline. Litmus can be used for this purpose, for we learned long since that litmus turns red with acids and blue with alkalis. But litmus is not exact enough. We need some substances which will change their tint when there is but a fraction of 1 per cent of free acid or free alkali present. Such a coloring matter is called an *indicator*, and chief among those used in this class of volumetric analysis are the following:

Phenolphthalein, red with alkalis, colorless with acids.
Methyl orange, yellow with alkalis, red with acids.
Methyl red, violet-red with acids and yellow with alkalis.

The new Pharmacopœia contains (Part II, p. 559) a full discussion of indicators which should be carefully read by the student.

Turning to the process, suppose we combine sodium hydroxide with sulfuric acid to a neutral salt. Absolutely pure sodium hydroxide is NaOH; molecular weight, 40.00. Absolutely pure sulfuric acid is H_2SO_4; molecular weight, 98.08. The molecular weights just given are estimated from the "exact" atomic weights given by the Pharmacopœia and not from the "round number" atomic weights found in elemental table on page 390.

The reaction between sodium hydroxide and sulfuric acid can be expressed by the following equation:

$$\begin{array}{ccccccc} 2NaOH & + & H_2SO_4 & = & Na_2SO_4 & + & 2H_2O. \\ 2 \times 40.00 & & 98.08 & & 142.05 & & 2 \times 18.015 \\ \text{or } 80.00 & & & & & & \text{or } 36.030 \end{array}$$

We see from the equation that absolute sodium hydroxide combines with absolute sulfuric acid in the proportion of 80.00 Gm. of the hydroxide to 98.08 Gm. of the acid, and were we to prepare solutions of these two bodies of such strength that equal volumes of the two solutions would exactly neutralize each other, the solutions would have to be prepared to the ratio of 80.00 to 98.08.

To make it plainer: were we to prepare a liter of solution containing exactly 80.00 Gm. absolute sodium hydroxide, a liter of solution of sulfuric acid to neutralize it would have to hold 98.08 Gm. of absolute acid; or if we prepared a solution of sodium hydroxide containing in 1 liter 40.00 Gm. of absolute hydroxide (½ of 80.00), then a liter of solution of sulfuric acid that would neutralize the hydroxide must contain one half of 98.08 or 49.04 Gm. of absolute sulfuric acid, and such is the strength of normal sulfuric acid, as reference to page 1007 will show. The foundation of acidimetric work is the strength of normal potassium hydroxide solution and normal sodium hydroxide solution, each of which represents in each liter of solution the number of grams of absolute hydroxide equal to the molecular weight of the substance employed. Thus, normal potassium hydroxide solution contains 56.10 Gm. of hydroxide to the liter, and normal sodium hydroxide contains 40 Gm. of hydroxide to the liter. On the other hand, the dibasic acids—sulfuric acid and oxalic acid—are made into normal volumetric solutions by using to a liter of solution, the number of grams of acids corresponding to *half* the molecular weight, since it takes only half a molecule (if the phrase is permissible) of either of these acids to neutralize 1 molecule of either of the two alkalis.

The use of a volumetric solution in testing is simple. The volumetric solution is poured into a graduated tube called a burette (see Fig. 24, p. 57), while the substance to be examined, after careful weighing, is dissolved and so placed that the contents of the burette can be gradually run into it. The indicator—usually phenolphthalein—is poured into the solution to be examined. Let us suppose this substance is an alkali: then the solution will be colored a beautiful red. Into this the volumetric solution is added gradually and stopped the moment that a drop of the reagent discharges the color of the solution, which will mean that the solution is no longer alkaline. Then a simple reckoning—amount of volumetric solution in burette *before*, minus amount *after*, dropping into tested solution, will give us the number of cubic centimeters of volumetric solution used in neutralizing the tested substance, and from these figures we can, by aid of the Pharmacopœia, estimate strength of the tested substance.

Applying these directions to the determination of potassium hydroxide, suppose we weigh out 1 Gm. of the chemical, dissolve it in water, and titrate it with normal sulfuric acid. We find the 1 Gm. of potassium hydroxide takes 16 cc. normal sulfuric acid (abbreviated nH_2SO_4) to neutralize it. From the equation—

$$\begin{array}{cccc} 2KOH + & H_2SO_4 = & K_2SO_4 + & 2H_2O \\ 112.20 & 98.08 & 174.25 & 36.030 \end{array}$$

we see that 98.08 Gm. absolute H_2SO_4 = 112.20 Gm. absolute KOH. We have learned that a liter of $nH_2SO_4 = \frac{98.08}{2}$ Gm. or 49.040 Gm. absolute H_2SO_4. Since 49.040 Gm. absolute $H_2SO_4 = \frac{112.20}{2}$ Gm., or 56.10 Gm. absolute KOH, we find that

1000 cc. nH_2SO_4 = 56.10 Gm. absolute KOH.
1 cc. nH_2SO_4 = 0.05610 Gm. absolute KOH.
Hence 16 cc. nH_2SO_4 = 16 × 0.05610 Gm. absolute KOH.
0.8976 Gm. absolute KOH.

Hence 1 Gm. potassium hydroxide we examined contained 0.8976 Gm. absolute KOH, and was therefore almost 90 per cent absolute.

Reference to U.S.P. (p. 575) will show that the factor "1 cc. nH_2SO_4 = 0.05610 Gm. absolute KOH" is found under the table of values of 1 cc. normal sulfuric acid V.S., and it need here be said that each particular value of 1 cc. normal acid found therein has been worked out by process of reasoning just given. The same obtains with the equivalent tables found under the several volumetric solutions, and incidentally it might be noted that 1 cc. of a normal acid or of normal alkali is represented as the same number of milligrams of the substance tested as the molecular weight of the substance if it be monobasic or monacid, half the molecular weight if it be dibasic or diacid, one third the molecular weight if it be tribasic or triacid.

The following volumetric solutions are used in acidimetry and alkalimetry:

NORMAL SULFURIC ACID VOLUMETRIC SOLUTION

$H_2SO_4 = 98.08$ 49.04 Gm. in 1000 cc.

Condensed Recipe.

Dilute 30 cc. of sulfuric acid U.S.P. with about 1020 cc. of distilled water. Standardize this either by titration with anhydrous sodium carbonate or (gravimetrically) by precipitation as barium sulfate. On estimating the strength of the latter, it is diluted with water to the exact normal strength, which is to be proved by a titration of the diluted product. In this and all other cases U.S.P. XI permits the analyst to either bring the solution to exactly standard strength or after ascertaining its exact strength to use the percentage factor representing the ratio between actual strength and standard normality. For details, see U.S.P., p. 563.

The Pharmacopœia also gives the equivalent value of normal sulfuric acid (the so-called *factor*) for a list of 18 chemicals assayed with that reagent. As an understanding of this factor is essential to the comprehension of volumetric methods it is worthy of explanation at this place.

On page 1005, it was pointed out that when sulfuric acid and sodium hydroxide were combined (as in a titration) each 49.04 Gm. of the absolute acid neutralized 40.00 Gm. of the absolute hydroxide. Then we learned that 1000 cc. of normal sulfuric acid contained 49.04 Gm. H_2SO_4 and therefore was the equivalent, in a titration, of 40.00 Gm. NaOH. It therefore follows that 1 cc. of normal sulfuric acid represents 40.00 ÷ 1000 or 0.04000 Gm. KOH and this we find is stated in the table of "equivalent values" (or factors) of normal sulfuric acid which is provided in the Pharmacopœia. The factor, of course, bears a direct relation to the molecular weight of the chemical in question depending, as do volumetric solutions, on the hydrogen value of the substance under consideration.

HALF-NORMAL SULFURIC ACID VOLUMETRIC SOLUTION

$H_2SO_4 = 98.08$ 24.52 Gm. in 1000 cc.

Condensed Recipe.

U.S.P. XI gives no specific directions as to preparation of this solution beyond the general statement (p. 563) that a half-normal solution is exactly one half the strength of a normal solution. A list of seventeen equivalent factors is given.

TENTH-NORMAL SULFURIC ACID VOLUMETRIC SOLUTION

$H_2SO_4 = 98.08$ 4.904 Gm. in 1000 cc.

Condensed Recipe.

Dilute 100 cc. of normal sulfuric acid with sufficient distilled water at the same temperature to measure 1000 cc. (see half-normal sulfuric acid).

The Pharmacopœia gives a list of equivalent factors for ten chemicals assayed with tenth-normal acid.

FIFTIETH-NORMAL SULFURIC ACID VOLUMETRIC SOLUTION

$H_2SO_4 = 98.08$ 0.9808 Gm. in 1000 cc.

Condensed Recipe.

Dilute 200 cc. of tenth-normal sulfuric acid with enough distilled water to make 1000 cc. (see half-normal sulfuric acid).

TENTH-NORMAL OXALIC ACID VOLUMETRIC SOLUTION

$H_2C_2O_4 + 2H_2O = 126.05$ 6.303 Gm. in 1000 cc.

Condensed Recipe.

Dissolve 6.45 Gm. reagent oxalic acid in enough distilled water to make 1000 cc. Standardize this with tenth-normal potassium permanganate and then dilute to exactly tenth-normal strength. For details, see U.S.P., p. 567.

The Pharmacopœia gives the factor for fourteen chemicals assayed with tenth-normal oxalic acid.

NORMAL HYDROCHLORIC ACID VOLUMETRIC SOLUTION

HCl = 36.47 36.47 Gm. in 1000 cc.

Condensed Recipe.

Mix 95 cc. of hydrochloric acid with enough distilled water to make 1000 cc. Standardize with either anhydrous sodium carbonate or with silver nitrate. Then dilute to exactly normal strength. For details, see U.S.P., p. 565.

The Pharmacopœia gives factors for twelve chemicals, when tested with normal hydrochloric acid.

HALF-NORMAL HYDROCHLORIC ACID VOLUMETRIC SOLUTION

HCl = 36.47 18.235 Gm. in 1000 cc.

Condensed Recipe.

Dilute 500 cc. of normal hydrochloric acid V.S. with enough water to make 1000 cc.

No factors are given; U.S.P. XI stating that the factors are identical with those given under half-normal sulfuric acid.

NORMAL POTASSIUM HYDROXIDE VOLUMETRIC SOLUTION

KOH = 56.10 56.10 Gm. in 1000 cc.

Condensed Recipe.

U.S.P. XI directs this only as an alternative solution; to be prepared in manner similar to the making of normal sodium hydroxide.

HALF-NORMAL ALCOHOLIC POTASSIUM HYDROXIDE VOLUMETRIC SOLUTION

KOH = 56.10 28.05 Gm. in 1000 cc.

Condensed Recipe.

Prepare a solution consisting of 35 Gm. potassium hydroxide, 20 cc. of distilled water and enough of aldehyde-free alcohol to make 1 liter. Standardize this by titration with *n*/2 HCl and then dilute with the purified alcohol to exactly half-normal strength. Directions are also given for preserving the finished solution. For details, see U.S.P., p. 569.

The Pharmacopœia also gives the factors for eight chemicals assayed with half-normal alcoholic potassium hydroxide V.S.

NORMAL SODIUM HYDROXIDE VOLUMETRIC SOLUTION

NaOH = 40.00 40 Gm. in 1000 cc.

Condensed Recipe.

Dissolve 45 Gm. sodium hydroxide in 950 cc. distilled water. Remove carbonates by addition of barium hydroxide. Titrate a portion of the clear fluid against potassium bitartrate or normal hydrochloric or sulfuric acid or potassium biphthalate and then dilute remainder to exact normal strength. For details, see U.S.P., p. 571.

The Pharmacopœia gives factors for twenty-three chemicals assayed with normal sodium hydroxide V.S.

HALF-NORMAL SODIUM HYDROXIDE VOLUMETRIC SOLUTION

NaOH = 40.00 20 Gm. in 1000 cc.

Condensed Recipe.

Dilute 500 cc. of exactly normal sodium hydroxide with enough recently boiled distilled water to make 1000 cc. (see half-normal sodium hydroxide). The Pharmacopœia gives factor for only one chemical assayed with *n*/2 HCl; acetylsalicylic acid. It is obvious that the factors for the half-normal solution are exactly one half of the factors for normal solution.

TENTH-NORMAL SODIUM HYDROXIDE VOLUMETRIC SOLUTION

NaOH = 40.00 4 Gm. in 1000 cc.

Condensed Recipe.

Dilute 100 cc. of exactly normal sodium hydroxide V.S. with enough recently boiled distilled water to make 1000 cc.

Of the three factors given in the Pharmacopœia, two are for those chemicals given under normal or half-normal sodium hydroxide. These factors are, of course, one tenth that of the normal or one fifth half-normal factors. The other one is eucaine hydrochloride and the factor in this case is *the molecular weight divided by 10,000.*

Provisions are also made for twentieth-normal and fiftieth-normal sodium hydroxide and for details concerning these the reader is referred to U.S.P., page 573. While potassium hydroxide volumetric solution was preferred in former Pharmacopœias the present U.S.P. directs the corresponding sodium hydroxide solutions; merely mentioning normal potassium hydroxide (56.10 Gm. in 1000 cc.) as an alternative solution.

TENTH-NORMAL BARIUM HYDROXIDE VOLUMETRIC SOLUTION

$Ba(OH)_2 + 8H_2O = 315.50$ 15.775 Gm. in 1000 cc.

Condensed Recipe.

Dissolve 18 Gm. crystallized barium hydroxide in 1000 cc. of recently boiled distilled water. After filtering, standardize with tenth-normal hydrochloric acid using phenolphthalein as indicator and dilute with freshly boiled distilled water to exactly tenth-normal strength. For details, including method of preservation, see U.S.P., p. 564.

The Pharmacopœia gives factors for seven chemicals titrated with tenth-normal barium hydroxide.

OFFICIAL CHEMICALS ASSAYED WITH NORMAL SODIUM HYDROXIDE

A definite weight of the substance is dissolved in or diluted with distilled water and is then titrated with the *n*NaOH. Indicator phenolphthalein in some cases; methyl orange in others. For details see U.S.P. XI.

The following chemicals are assayed by this method:

Acetic acid
Diluted acetic acid
Glacial acetic acid
Citric acid
Hydrochloric acid
Diluted hydrochloric acid
Hypophosphorous acid
Nitric acid
Sulfuric acid
Diluted sulfuric acid
Tartaric acid
Trichloracetic acid
Potassium bitartrate

The following are assayed similarly but sodium chloride is added as a buffer salt:

Phosphoric acid
Diluted phosphoric acid
Sodium biphosphate

The following are assayed similarly but glycerin is added to insure complete ionization:

Boric acid and its ointment

As these assays omit all calculations of results it is advisable here to state that the mathematical equation used in calculating strength is

$$\frac{\text{mils } n\text{NaOH used} \times \text{proper factor} \times 100}{\text{weight of assayed chemical}} = \text{percentage.}$$

Referring to the U.S.P. table of values under normal sodium hydroxide on page 572, it will be seen that 1 cc. of the volumetric solution equals 0.03647 Gm. absolute hydrochloric acid. This represents the "proper factor" mentioned in the equation and each time a chemical is assayed with a volumetric solution, refer to the table of factors for that solution found in the Pharmacopœia, and discussed at some length on page 1007 of this book.

The following chemicals are assayed with *n*NaOH by the method known as a "residual assay." The U.S.P. assay for chloral hydrate directs 4 Gm. of the chemical be dissolved in distilled water, then treated with 30 cc. of *n*NaOH and then titrated with nH_2SO_4; phenolphthalein being the indicator.

If exactly 4 Gm. of chloral hydrate were taken and the excess alkali took 6 cc. of normal acid for neutralization, then it means that 30 − 6 or 24 cc. of *n*NaOH were used by the chloral hydrate. If, as stated above, each gram of chloral hydrate corresponds to 6.02 cc. of *n*NaOH then it follows that the 24 cc. used in the reaction meant about 4 Gm. (exactly 3.9696 Gm.) of chloral hydrate.

Official chemicals, other than chloral hydrate, thus assayed are:

Acetylsalicylic acid
Lactic acid
Solution of formaldehyde
Aromatic sulfuric acid

OFFICIAL CHEMICALS ASSAYED WITH TENTH-NORMAL BARIUM HYDROXIDE V.S.

Benzoic Acid.—Accurately weigh about 0.5 Gm. well-dried benzoic acid, dissolve in 25 cc. of neutral diluted alcohol and titrate with $n/10$ $Ba(OH)_2$. Indicator, phenolphthalein.

The following chemicals are assayed in a similar fashion:

Salicylic acid
Ammonium benzoate
Ammonium salicylate
Caffeine sodio-benzoate
Theobromine sodio-salicylate

OFFICIAL CHEMICALS ASSAYED WITH NORMAL SULFURIC ACID V.S.

Ammonia Water.—Weigh about 5 cc. of ammonia water, in 25 cc. distilled water and titrate with nH_2SO_4. Indicators, phenolphthalein and methyl red T S.

The following chemicals are thus assayed:

Stronger ammonia water
Potassium bicarbonate
Potassium carbonate
Potassium hydroxide
Sodium bicarbonate
Monohydrated sodium carbonate
Sodium hydroxide

The following chemicals are assayed with normal H_2SO_4 by "residual titration"; that is, the chemical is dissolved in a known excess of the normal acid and the solution is then titrated with normal NaOH. Thus in the case of ammonium carbonate (see U.S.P., p. 54) we start in with 50 cc. nH_2SO_4, which, of course, would require 50 cc. *n*NaOH for neutralization. If we start in with exactly 2 Gm. ammonium carbonate and dissolve this in 50 cc. nH_2SO_4 and if on titration 14 cc. *n*NaOH were required for neutralization, it follows that 50 − 14 or 36 cc. nH_2SO_4 were used to neutralize 2 Gm. ammonium carbonate. U.S.P. XI (p. 54) states that ammonium carbonate represents between 30 and 32 per cent of ammonia, NH_3. On page 54 of U.S.P. XI, we find that each cubic centimeter of nH_2SO_4 represents 0.01703 Gm. NH_3; hence 36 cc. nH_2SO_4 represents 36 × 0.01703 or 0.61308 Gm. absolute NH_3. This would indicate that our sample of ammonium carbonate represents

$$\frac{0.61308}{2.00000} \times 100 \text{ per cent, or } 30.65 \text{ per cent ammonia.}$$

The chemicals assayed by residual alkalimetric titrations are tabulated below:

Ammonium carbonate
Aromatic spirit of ammonia
Magma of magnesia
Magnesium carbonate
Magnesium oxides
Methenamine
Solution of ammonium acetate
Zinc oxide

OFFICIAL CHEMICALS ASSAYED WITH HALF-NORMAL SULFURIC ACID V.S.

This reagent is used in assaying the alkali salts of organic acids and the manipulation is described in the Pharmacopœia (p. 439). The test may be summarized as follows:

Outline of Assays for Alkali Salts of Organic Acids.—Accurately weigh about 2 Gm. of the salt, then carbonize at red heat, until a white residue remains. Then dissolve in water; add 50 cc. $n/2$ H_2SO_4 and titrate residual acid with $n/2$ NaOH. Indicator, methyl orange.

The following chemicals and preparations are thus tested:

Potassium acetate
Potassium citrate
Potassium and sodium tartrate
Sodium acetate
Sodium citrate

Seidlitz powder is assayed with half-normal sulfuric acid both for sodium bicarbonate and for potassium and sodium tartrate. The first assay is a residual titration; while the second one is the one prescribed for alkali salts of organic acids.

OFFICIAL CHEMICALS ASSAYED WITH TENTH-NORMAL SULFURIC ACID

Solution of Calcium Hydroxide.—Titrate 50 cc. of the solution with $n/10$ H_2SO_4. Indicator, phenolphthalein. Strength, not less than 0.14 per cent $Ca(OH)_2$.

Zinc stearate is assayed in similar fashion, while *tablets of glyceryl trinitrate* are oxidized to ammonia by use of potassium permanganate, the gas distilled into $n/50$ H_2SO_4 and the residual acid is then titrated with $n/50$ NaOH.

OFFICIAL CHEMICALS ASSAYED WITH NORMAL HYDROCHLORIC ACID V.S.

Sodium cacodylate is assayed by a direct simple titration with nHCl.

OFFICIAL CHEMICALS ASSAYED WITH HALF-NORMAL HYDROCHLORIC ACID V.S.

Two chemicals—*sodium benzoate* and *sodium salicylate*, are assayed with $n/2$ HCl by complicated processes. For details see U.S.P. XI.

IODOMETRY

By this term we mean those volumetric assays in which we use volumetric solution of iodine or volumetric solution of sodium thiosulfate, or both.

As already explained (p. 426), iodine in solution is decolorized by use of sodium thiosulfate, and this decoloration, like all chemical actions, takes place between definite proportions of the two chemicals, the equation being:

$$\underset{\substack{2 \times 126.92 \\ \text{or } 253.84}}{I_2} + \underset{\substack{2 \times 248.19 \\ \text{or } 496.38}}{2Na_2S_2O_3 5H_2O} = 2NaI + Na_2S_4O_6 + 10H_2O.$$

We see from this equation that 253.84 Gm. iodine take 496.28 Gm. crystallized sodium thiosulfate to complete the reaction—to completely decolorize it. Therefore, if we prepare a decinormal iodine solution (12.69 Gm. to the liter), we can calculate that this 12.69 Gm. iodine will take $\frac{12.69}{253.84} \times 496.38 = 24.819$ Gm. sodium thiosulfate, which amount is exactly the quantity needed to make 1 liter of decinormal sodium thiosulfate solution. Hence equal volumes of the two decinormal solutions exactly react with each other.

In titrating iodine solution with thiosulfate solution we either add the thiosulfate solution until the brown-yellow color of the iodine is discharged, or, better still, we use as indicator starch mucilage, which we have already learned strikes a deep blue color with iodine (p. 426). The moment all the iodine in a given solution is taken up by the thiosulfate, the blue color is discharged.

Were the sole use of iodine solution and thiosulfate solution the estimation of the strength of these two chemicals, the value of iodometry would be limited. Far more extended, however, is its application, because of the fact that iodine, when treated with reducing agents, is converted into hydriodic acid or iodides, as shown in the following equations:

(*a*) $I_2 + \underset{\text{Sulphurous oxide.}}{SO_2} + 2H_2O = \underset{\text{Hydriodic acid.}}{2HI} + \underset{\text{Sulphuric acid.}}{H_2SO_4}.$

(*b*) $2I_2 + \underset{\text{Arsenous oxide.}}{As_2O_3} + 2H_2O = 4HI + \underset{\text{Arsenic oxide.}}{As_2O_5}.$

(*c*) $I_2 + Fe = FeI_2,$

and thus loses its ability to color starch mucilage blue. Hence if we treat a known excessive quantity of iodine solution with any of the reducing agents just mentioned, by titrating the excess of iodine remaining after the reaction with thiosulfate solution, we can calculate how much iodine was used by the reducing chemical and thus estimate the amount of chemical itself.

On the other hand, potassium iodide when treated with oxidizing agents liberates a proportional quantity of its iodine, as is shown in the following equations:

(*d*) $KI + Br = KBr + I.$

(*e*) $KI + Cl = KCl + I.$

(*f*) $3KI + \underset{\text{Chromic oxide.}}{CrO_3} + 6HCl = CrCl_3 + 3KCl + 3H_2O + I_3.$

(*g*) $KI + \underset{\text{Ferric chloride.}}{FeCl_3} = FeCl_2 + KCl + I.$

and by titrating this liberated iodine with thiosulfate solution the amount of the oxidizing agent can be deduced.

The pharmacopœial preparation of decinormal iodine solution and of decinormal thiosulfate solution are given below.

TENTH-NORMAL IODINE VOLUMETRIC SOLUTION

I = 126.92 12.692 Gm. in 1000 cc.

Condensed Recipe.

Dissolve exactly 12.75 Gm. purified iodine in a solution of 36 Gm. potassium iodide in 100 cc. of distilled water; finally diluting to 1000 cc. The iodine solution is then standardized with tenth-normal sodium thiosulfate solution (see p. 1011). For details, see U.S.P., p. 567.

The Pharmacopœia gives equivalent factors for sixteen chemicals assayed with tenth-normal iodine V.S.

TENTH-NORMAL SODIUM THIOSULFATE VOLUMETRIC SOLUTION

$Na_2S_2O_3 + 5H_2O$ = 248.19 24.819 Gm. in 1000 cc.

Condensed Recipe.

Dissolve about 26 Gm. sodium thiosulfate and 0.2 Gm. of sodium carbonate in enough distilled water to make 1 liter, standardize the solution by titration with tenth-normal potassium dichromate, potassium iodide and sulfuric acid (see below) and then dilute the solution, so that each cubic centimeter corresponds with 1 cc. of the dichromate solution. For details, see U.S.P., p. 573.

The Pharmacopœia gives factors for seventeen chemicals assayed with tenth-normal sodium thiosulfate V.S.

TWO-HUNDREDTH-NORMAL SODIUM THIOSULFATE VOLUMETRIC SOLUTION

$Na_2S_2O_3 + 5H_2O = 248.19$ 1.2410 Gm. in 1000 cc.

Condensed Recipe.

Dilute 25 cc. of tenth-normal sodium thiosulfate V.S. with enough distilled water to make a liter. This solution may be standardized with tenth-normal potassium dichromate V.S., potassium iodide and sulfuric acid (see half-normal sulfuric acid (p. 1007).

The Pharmacopœia gives the equivalent factor for elemental iodine, for iodine from thyroid glands and for glyceryl trinitrate.

The arithmetic of the standardization of the tenth-normal thiosulfate solution is worthy of explanation.

On page 1012 (equation *f*) we find that chromium trioxide liberates iodine from potassium iodide. Potassium dichromate in acid solution does likewise, the equation being

$$\underset{294.21}{K_2Cr_2O_7} + 6KI + 6H_2SO_4 = Cr_2(SO_4)_3 + 3K_2SO_4 + 6H_2O + \underset{6 \times 126.9}{3I_2}$$

From this equation, we learn that

$$\begin{aligned} 6 \times 126.9 \text{ Gm. I} &= 294.21 \text{ Gm. } K_2Cr_2O_7 \\ 126.9 \text{ Gm. I} &= 49.035 \text{ Gm. } K_2Cr_2O_7 \\ 12.69 \text{ Gm. I} &= 4.9035 \text{ Gm. } K_2Cr_2O_7. \\ \text{Hence 1000 cc. } n/10 \text{ iodine (12.69 Gm. to the liter)} &= 4.9035 \text{ Gm. } K_2Cr_2O_7 \\ 1 \text{ cc. } n/10 \text{ iodine} &= 0.0049035 \text{ Gm. } K_2Cr_2O_7. \end{aligned}$$

As 1 cc. of tenth-normal thiosulfate V.S. is necessary to decolorize 1 cc. of tenth-normal iodine V.S. and as 1 cc. of tenth-normal dichromate V.S. contains 0.0049035 Gm. $K_2Cr_2O_7$, it follows that in the thiosulfate assay each cubic centimeter of an exactly tenth-normal thiosulfate V.S. corresponds to 1 cc. of tenth-normal dichromate V.S.

TWENTIETH-MOLAR POTASSIUM IODATE VOLUMETRIC SOLUTION

$KIO_3 = 214.02$.   10.701 Gm. in 1000 cc.

Condensed Recipe.

Dissolve 10.701 Gm. of reagent potassium iodate, previously dried to constant weight at 110° C. in sufficient distilled water to make 1000 cc.

The Pharmacopœia gives factors for three chemicals titrated with twentieth-molar potassium iodate.

OFFICIAL DIRECT ASSAYS WITH TENTH-NORMAL SODIUM THIOSULFATE V.S.

Iodine.—Accurately weigh about 0.5 Gm. powdered iodine and dissolve in an aqueous solution of potassium iodide. Dilute this with water and titrate with $n/10$ thiosulfate. Indicator, starch paste.

Like the foregoing are run:

Tincture of iodine
Compound solution of iodine
Mild tincture of iodine

OFFICIAL DIRECT ASSAY WITH TENTH-NORMAL IODINE V.S.

Sodium Thiosulfate.—Accurately weight about 0.5 Gm. sodium thiosulfate, dissolve in distilled water and titrate with $n/10$ iodine. Indicator, starch paste.

Similar methods are employed in assaying:

Arsenic trioxide
Arsenic tri-iodide
Solution of arsenous acid
Antimony and potassium tartrate
Solution of potassium arsenite
Tryparsamide

There are two residual titrations in which a definite excess of $n/10$ iodine is employed and the surplus of free iodine remaining after the reduction reaction is then titrated with $n/10$ thiosulfate. In the calomel assay if we take exactly 0.7 Gm. of that chemical, treat it with 50 cc. of $n/10$ iodine and find on residual titration that the excess iodine requires 20.5 cc. $n/10$ thiosulfate for decolorization, it means that 50 − 20.5 or

29.5 $n/10$ iodine were used for reducing 0.7 Gm. calomel. The two chemicals thus assayed are:

Mild mercurous chloride
Yellow mercurous oxide

An iodine assay of special character is that provided for acetone.

This assay is based upon the fact that acetone plus alkali plus iodine yields iodoform (p. 647). A known excess of $n/10$ iodine is employed in assay and the free iodine, remaining after the acetone has been converted into iodoform, is titrated with $n/10$ thiosulfate.

OFFICIAL OXIDATION ASSAY WITH TENTH-NORMAL SODIUM THIOSULFATE V.S.

These assays involve the treatment of the chemical with potassium iodide and acetic acid and final titration of the liberated iodine with $n/10$ thiosulfate. For details in each case see U.S.P.

In three assays, the iodine or iodide is oxidized to iodate by treatment with potassium permanganate. The resulting iodate is then treated with potassium iodide and sulfuric acid and the liberated iodine is then titrated with $n/10$ thiosulfate V.S.

Thymol iodide
Calcium iodobehenate
Ointment of iodine

In two assays, the trivalent arsenic of the chemicals is converted into arsenic acid H_3AsO_4 and this in turn liberates iodine from potassium iodide, which is then titrated with $n/10$ thiosulfate.

Arsphenamine
Neoarsphenamine

OFFICIAL ASSAY WITH TWO-HUNDREDTH-NORMAL SODIUM THIOSULFATE V.S.

Dried Thyroids.—Fuse 1 Gm. dried thyroids with a mixture of potassium carbonate, sodium carbonate and potassium nitrate. When the mixture is completely carbonized dissolve the residue in warmed distilled water. Then add solution of chlorinated soda and phosphoric acid, dilute with water and boil for one-half hour. After cooling the liquid, add to it potassium iodide and titrate the liberated iodine with $n/200$ $Na_2S_2O_3$.

The chemicals and preparations so assayed are:

Solution of sodium hypochlorite
Chloramine
Diluted solution of sodium hypochlorite
Dichloramine
Copper sulfate

The assays which follow resemble the five just given except that the iodine is liberated from potassium iodide by treatment with hydrochloric acid instead of acetic acid.

Solution of ferric chloride
Tincture of ferric chloride
Solution of ferric sulfate
Iron and ammonium citrate
Green iron and ammonium citrate
Ferric phosphate
Chromium trioxide

The *nitrite assay* as given in U.S.P. XI (pp. 457, 458) involves the liberation of iodine from potassium iodide upon addition of a nitrite. The iodine is liberated in molecular proportions, and is then titrated with $n/10$ thiosulfate. The following chemicals are thus assayed:

Amyl nitrite
Spirit of ethyl nitrite
Spirit of glyceryl trinitrate

This assay, like the one for thymol iodide, is based upon the conversion of the organic into inorganic iodide, the oxidization of this to iodate, the treatment of this with potassium iodide and phosphoric acid; and the final titration of the liberated iodine with *n*/200 thiosulfate V.S.

OFFICIAL ASSAYS WITH TWENTIETH-MOLAR POTASSIUM IODATE

Soluble Iodophthalein.—Fuse with anhydrous sodium carbonate, dissolve fused mass in distilled water and filter. Add hydrochloric acid to the filtrate and titrate with *m*/20 KIO_3.

Similar methods are employed in the assays of:

Chiniofon powder

Iodized oil

The following are assayed by titration of an aqueous solution of the salt mixed with hydrochloric acid and chloroform with *m*/20 KIO_3. For details see U.S.P. XI.

Potassium iodide

Sodium iodide

OXIDATION ASSAYS WITH TENTH-NORMAL POTASSIUM PERMANGANATE V.S.

We have already learned (p. 414) that potassium permanganate is a powerful oxidizer, and that a solution in the process of oxidation loses its characteristic purple or rose tint—becomes decolorized. This phenomenon is employed in the volumetric determination of oxidizable substances, known quantities of such substances being added to volumetric solution of potassium permanganate until a permanent pink tint ensues. In other cases advantage is taken of the fact that oxalic acid decolorizes potassium permanganate, and by mixing chemicals that react with oxalic acid with a known quantity of volumetric solution of that acid and titrating the excess of the acid with permanganate, the quantity of acid used in combining with the particular chemical can be deduced and the amount of the chemical calculated.

Before discussing the arithmetic of such calculation it may be well to give an outline of the official method of making decinormal permanganate solution:

TENTH-NORMAL POTASSIUM PERMANGANATE VOLUMETRIC SOLUTION

$KMnO_4$ = 158.03. 3.161 Gm. in 1000 cc.

Condensed Recipe.

Mix 3.3 Gm. potassium permanganate U.S.P. in 1000 cc. of distilled water and boil about 5 minutes. Stopper the flask, let stand two days, and then filter through asbestos. Then dilute to exactly tenth-normal strength with a special distilled water, which has been treated with permanganate before being distilled. The solution is then standardized against reagent sodium oxalate. For details, see U.S.P., p. 569.

The Pharmacopœia also gives equivalent factors for twelve chemicals assayed with tenth-normal potassium permanganate V.S.

It will be seen from the above outline that the potassium permanganate solution is standardized by the use of sodium oxalate.

The reaction of this combination is as follows:

$$\underset{\substack{2 \times 158.03 \\ \text{or } 316.06}}{2KMnO_4} + \underset{\substack{5 \times 134.0 \\ \text{or } 670.0}}{5Na_2C_2O_4} + 8H_2SO_4 = K_2SO_4 + 2MnSO_4 + 5Na_2SO_4 + 10CO_2 + 8H_2O$$

It will be seen from this equation, that 670 Gm. sodium oxalate decolorizes 316.06 Gm. potassium permanganate. The pharmacopœial monograph states that each cubic centimeter of *n*/10 permanganate is equivalent to 0.0067 Gm. sodium oxalate. Then a liter (1000 cc.) of *n*/10 permanganate is equivalent to 6.700 Gm. sodium oxalate. The equation just given shows that 670 Gm. sodium oxalate represents 316.06 Gm. permanganate; hence 6.7 Gm. oxalate is equivalent to 3.16 Gm. permanganate; the obvious conclusion therefore is that a liter of *n*/10 permanganate should contain 3.16 Gm. $KMnO_4$.

At first glance it seems erroneous to call the permanganate solution containing in a liter the number of grams equivalent to one-fiftieth its molecular weight a decinormal solution, and it might here be stated that this conception is hard to comprehend unless we adopt the double formula of permanganate, $K_2Mn_2O_8$. If we take this double formula to express 1 molecule; if we appreciate that $K_2Mn_2O_8$ liberates 5 atoms oxygen in oxidation, viz.,

$$K_2Mn_2O_8 + 3H_2SO_4 = 2MnSO_4 + K_2SO_4 + 3H_2O + 5O;$$

if we appreciate that this liberation of 5 atoms of oxygen really means combination of 10 atoms of hydrogen, viz.,

$$10H + 5O = 5H_2O,$$

and, lastly, if we remember that the foundation of the arithmetic of volumetric testing is the quantity of substance that combines with or replaces 1 atom of hydrogen, we will see that the true normal solution of permanganate contains the amount with which 1 atom of hydrogen will combine—that is, $\frac{1}{10}$ of 316.06—and that the decinormal solution must contain in 1 liter $\frac{1}{100}$ of 316.06 Gm.

That this reasoning is sound is proved by the fact that a decinormal solution containing 31.6 Gm. permanganate to the liter combines with equal volumes of other decinormal solutions, such as *n*/10 oxalic acid and *n*/10 thiosulfate.

Referring to the table given above, showing the equivalent values of 1 cc. of *n*/10 permanganate, we find that while *n*/10 $K_2Mn_2O_8$ equals as many milligrams of permanganate as its molecular weight divided by 100, 1 cc. represents of the ferrous salts and hydrogen dioxide as many milligrams as the molecular weight in each case divided by 10; while with the substances, calcium oxide, oxalic acid, and sodium nitrite, 1 cc. of *n*/10 permanganate represents as many milligrams as the molecular weight divided by 20. These can be best explained by a typical equation from each class:

(*a*) $10FeSO_47H_2O + K_2Mn_2O_8 + 8H_2SO_4 = 5Fe_2(SO_4)_3 + 2MnSO_4 + K_2SO_4 + 15H_2O.$
10×278.01 316.06
or 2780
We see that 316.06 Gm. $KMnO_4$ = 2780 Gm. $FeSO_47H_2O$.
3.1606 Gm. $KMnO_4$
or 1000 cc. *n*/10 $KMnO_4$ = 27.80 Gm. $FeSO_47H_2O$
and that 1 cc. *n*/10 $KMnO_4$ = 0.0278 Gm. $FeSO_47H_2O$.

(*b*) $5NaNO_2 + K_2Mn_2O_8 + 3H_2SO_4 = 5KNO_3 + 2MnSO_4 + K_2SO_4 + 3H_2O.$
5×69.10 316.06
or 345.50
We see that 316.06 Gm. $KMnO_4$ = 345.50 Gm. $NaNO_2$
3.1606 Gm. $KMnO_4$
or 1000 cc. *n*/10 $KMnO_4$ = 3.4550 Gm. $NaNO_2$.
and that 1 cc. *n*/10 $KMnO_4$ = 0.00345 Gm. $NaNO_2$.

That is, while chemicals of the type "*a*" in oxidizing take up 1 atom of oxygen to every 2 molecules of the oxidized chemical, chemicals of type "*b*" combine with oxygen in the proportion of 1 atom of oxygen to each molecule.

It will, of course, be remembered that 1 molecule $K_2Mn_2O_8$ yields 5 atoms of oxygen, and these 5 atoms combine with 10 molecules of chemicals of type "*a*" and with 5 molecules of chemicals of type "*b*."

OFFICIAL ASSAYS MADE WITH TENTH-NORMAL PERMANGANATE V.S.

Solution of Hydrogen Dioxide.—Accurately weigh about 2 Gm. solution of hydrogen dioxide, dilute with water, acidulate with diluted sulfuric acid and then titrate with n/10 $KMnO_4$.

This reaction differs from either equation given on page 1016 inasmuch as both hydrogen dioxide and permanganate liberate oxygen, which passes off as gas, as shown in the following equation:

$$5H_2O_2 + K_2Mn_2O_8 + 3H_2SO_4 = 5O_2 + K_2SO_4 + 2MnSO_4 + 8H_2O.$$

The following chemicals are assayed in a similar fashion:

Sodium perborate
Ferrous sulfate
Reduced iron

In the reduced iron assay, the chemical is boiled with mercuric chloride solution which converts all of the iron into ferrous chloride which is then assayed by titration with n/10 permanganate.

The following are performed by residual titration; the chemical being treated with an excess of n/10 oxalic acid which combines with the metal found in the chemical. The surplus oxalic acid is then titrated with n/10 permanganate V.S.

Calcium bromide
Calcium chloride
Precipitated calcium carbonate
Calcium hydroxide
Prepared chalk
Calcium gluconate
Calcium lactate
Lead acetate
Potassium permanganate

In the case of calcium gluconate and lactate, the calcium oxalate is collected on a filter, is washed and is finally titrated with permanganate.

For details, see U.S.P., pp. 100 and 102. Finally, in the case of two official chemicals:

Sodium nitrite
Potassium chlorate

the residual titrations are performed by intricate processes that should be studied in the pharmacopœial text.

OXIDATION ASSAYS WITH TENTH-NORMAL POTASSIUM DICHROMATE V.S.

As the operation is so closely similar to assaying with potassium permanganate, and as only three official preparations are directed to be tested by this method, we need not take much time for its discussion.

All that is necessary to state is that the oxidation with dichromate is limited to ferrous salts and to the liberation of iodine from potassium iodide in standardizing sodium thiosulfate V.S. Further, that the oxidizing action of dichromate is that shown in the following typical equation:

$$K_2Cr_2O_7 + 4H_2SO_4 = K_2SO_4 + Cr_2(SO_4)_3 + 4H_2O + O_3.$$

In other words, while *2* molecules nitric acid in oxidation processes give 3 atoms of oxygen (see p. 447), 1 molecule dichromate gives 3 atoms of oxygen also. Hence when dichromate can be substituted for nitric acid in oxidations, 1 molecule does the work of 2 molecules of acid.

Since 1 molecule $K_2Cr_2O_7$ yields 3 atoms of oxygen, 1 molecule $K_2Cr_2O_7$ is the equivalent of 6 atoms of hydrogen; hence normal potassium dichromate solution would contain in 1000 cc. as many grams $K_2Cr_2O_7$ as the molecular weight (294.2) divided by 6; that is, 49.035 Gm. Therefore decinormal dichromate V.S. contains 4.9035 Gm. $K_2Cr_2O_7$ to the liter, as is shown in the pharmacopœial recipe which follows:

TENTH-NORMAL POTASSIUM DICHROMATE VOLUMETRIC SOLUTION

$K_2Cr_2O_7 = 294.21$ 4.9035 Gm. in 1000 cc.

Condensed Recipe.

Dissolve 5 Gm. reagent potassium dichromate in enough distilled water to make 1000 cc. and standardize against potassium iodide and tenth-normal sodium thiosulfate.

The Pharmacopœia describes its use in estimating ferrous salts and gives its equivalent factors, for four chemicals; these factors, of course, the same as the thiosulfate factors for the same chemicals. For details, see U.S.P., p. 568.

OFFICIAL ASSAYS MADE WITH TENTH-NORMAL POTASSIUM DICHROMATE V.S.

The Pharmacopœia directs the use of dichromate V.S. in the case of two preparations:

Mass of ferrous carbonate Pills of ferrous carbonate

For details U.S.P. XI should be consulted.

VOLUMETRIC ASSAYS WITH SILVER NITRATE AND POTASSIUM THIOCYANATE

This class of assays is based either on the ability of silver nitrate to precipitate in definite proportions with the halogens, as shown in the following equation:

$$\underset{169.89}{AgNO_3} + \underset{58.45}{NaCl} = AgCl + NaNO_3,$$

or with potassium thiocyanate, viz.,

$$\underset{169.89}{AgNO_3} + \underset{76.107}{NH_4SCN} = AgSCN + NH_4NO_3.$$

From the above equations and appended molecular weights we see that 169.89 Gm. $AgNO_3$ = 58.45 Gm. NaCl,
and that 169.89 Gm. $AgNO_3$ = 76.107 Gm. NH_4SCN.

Since $n/10$ $AgNO_3$ contains 16.989 Gm. $AgNO_3$ to 1000 cc.
and $n/10$ $AgNO_3$ contains 0.01699 Gm. $AgNO_3$ to 1 cc.,
therefore 1 cc. $n/10$ $AgNO_3$ = 0.005845 Gm. NaCl
and 1 cc. $n/10$ $AgNO_3$ = 0.0076107 Gm. NH_4SCN.

As fully explained below, the indicator used when assaying halogens with silver nitrate is potassium chromate, it striking a red, permanent tint (silver chromate) only after the addition of just enough silver nitrate completely to precipitate the halogen. When testing with thiocyanate, ferric alum is used as indicator, it forming red ferric thiocyanate only after all the silver is precipitated.

The preparation of the volumetric solutions is given below:

TENTH-NORMAL SILVER NITRATE VOLUMETRIC SOLUTION

$AgNO_3 = 169.89$ 16.989 Gm. in 1000 cc.

Condensed Recipe.

Dissolve 17.006 Gm. of reagent silver nitrate previously dried at 110° C. in sufficient distilled water to make 1000 cc.

A second method is to dissolve about 17.5 Gm. of silver nitrate U.S.P. in 1000 cc. of distilled water and standardize by gravimetric analysis. For details, see U.S.P., p. 570.

TENTH-NORMAL AMMONIUM THIOCYANATE V.S.

$NH_4SCN = 76.107$ 7.6107 Gm. in 1000 cc.

Condensed Recipe.

Dissolve about 8 Gm. of reagent ammonium thiocyanate in 1000 cc. of distilled water. Standardize against $n/10$ $AgNO_3$ V.S. For details, see U.S.P., p. 563.

The Pharmacopœia gives equivalent factors for five chemicals assayed with ammonium thiocyanate.

VOLUMETRIC ASSAY WITH TENTH-NORMAL SILVER NITRATE V.S.

Oil of Bitter Almond is assayed for HCN with $n/10$ silver nitrate by direct titration. This assay is based on the formation of a soluble double salt (AgCNKCN), which is decomposed the minute an excess of silver is added. Potassium iodide accentuates the reaction.

VOLUMETRIC ASSAYS WITH TENTH-NORMAL AMMONIUM THIOCYANATE V.S.

Silver Nitrate.—Accurately weigh about 0.8 Gm. well-dried nitrate, dissolve in distilled water, add nitric acid and ferric alum solution and titrate with $n/10$ NH_4SCN.

Toughened Silver Nitrate.—Accurately weigh about 0.8 Gm. moulded nitrate mixed with distilled water, filter off the silver nitrate solution, washing the residue and the filter with distilled water, add to the filtrate nitric acid and ferric alum T.S. and then titrate with $n/10$ NH_4SCN.

The following chemicals are similarly assayed, it being necessary however in each case to dissolve the compound in nitric acid (the salicylate with a mixture of sulfuric and nitric acids) in order to effect solution. For details see U.S.P.

Mercury
Mercury with chalk
Yellow mercuric oxide
Mercuric salicylate
Mercuric succinimide
Silver proteins (titration of ash)

Mass of Mercury.—Accurately weigh about 0.5 Gm. mass of mercury, add a mixture of sulfuric and nitric acids and heat on a sand bath until a clear colorless solution results. Then oxidize the solution with permanganate solution, decomposing excess of permanganate with oxalic acid solution. This solution is then titrated with $n/10$ NH_4SCN, ferric alum being used as indicator.

In the foregoing assay, the heating of the mass with sulfuric and nitric acids is to destroy the organic matter with which the mercury is admixed. The addition of potassium permanganate solution is to confer any possible mercurous salt into the mercuric form. The rest of the assay is a direct thiocyanate titration.

Mercurial Ointment and Stronger Mercurial Ointment.—Accurately weigh 1 Gm. of the ointment, digest in nitric acid and water until a colorless solution of mercuric nitrate is obtained and then titrate with $n/10$ NH_4SCN, ferric alum being used as indicator. For details, see U.S.P., p. 420.

VOLUMETRIC ASSAYS WITH TENTH-NORMAL SILVER NITRATE V.S. AND TENTH-NORMAL AMMONIUM THIOCYANATE V.S.

Potassium Bromide.—Accurately weigh about 0.4 Gm. of the bromide, dissolve in about 50 cc. of distilled water, add 50 cc. of $n/10$ $AgNO_3$, 2 cc. of ferric alum T.S. and 2 cc. of nitric acid. Then titrate excess of silver with $n/10$ NH_4SCN. For details, see U.S.P., p. 298.

In this assay an excess of volumetric solution of silver nitrate is added, and after precipitation of silver bromide, the silver still remaining in solution is titrated with ammonium thiocyanate. The calculations whereby the figures given in the assay are obtained are as follows:

By reference to the equivalent tables on page 571 of the U.S.P. we find:

1 cc. $n/10$ $AgNO_3$ = 0.01190 Gm. KBr, or reversed, 0.01190 Gm. KBr takes 1 cc. $n/10$ $AgNO_3$. Then 1.00 Gm. KBr takes $\frac{10{,}000}{1{,}190} \times 1$ cc. $n/10$ $AgNO_3$, or 1.00 Gm. KBr takes about 84 cc. $n/10$ $AgNO_3$.

The other chlorides and bromides are titrated in similar fashion:

Sodium bromide
Sodium chloride
Ammonium bromide
Ammonium chloride

For details, see U.S.P.

Liniment of Chloroform and *Spirit of Chloroform* are submitted to complicated treatment involving the separation and decomposition of the chloroform, followed by residual titration of the resulting chloride with $n/10$ $AgNO_3$ and $n/10$ KSCN. For details, see U.S.P.

Potassium Nitrate.—Accurately weigh about 0.4 Gm. well-dried nitrate, dissolve in 10 cc. of hydrochloric acid, evaporate the solution to dryness on a water bath; repeat treatment with hydrochloric acid and evaporation, then dissolve in water and assay for chlorides, as above.

Similar residual assays are provided for the following official chemicals:

Diluted hydriodic acid
Syrup of hydriodic acid
Syrup of ferrous iodide
Volatile oil of mustard
Black mustard

CHAPTER LVI

ASSAYS OF ORGANIC SUBSTANCES

PHARMACEUTIC ASSAYING

ASIDE from the volumetric determination of organic acids described on page 1010 under Alkalimetry, there are several forms of volumetric assays peculiar to organic substances. These include estimation of saponification number and iodine absorption number of oils and fats; the acid number of resins; that modification of acidimetry applied in alkaloidal assays, as well as the special assay of sugars with Fehling's solution and of phenol with Koppeschaar's solution. These will be considered in this chapter.

ALKALOIDAL ASSAYS

OFFICIAL ASSAYS IN WHICH THE ALKALOID OR PRINCIPLE IS WEIGHED

As already outlined on page 995, the official assays for alkaloids naturally fall into two groups—the isolation of the alkaloid and the determination of the isolated alkaloid either by direct weighing or by determination by titration with decinormal or centinormal acid (or indirectly by titrating excess of acid with volumetric alkali solution). As already mentioned, the alkaloid is isolated by extracting the drug with aqueous (either plain or acidulated) media, the alkaloid set free by addition of alkali, and the freed alkaloid separated by "shaking out" with a solvent immiscible with water.

The Pharmacopœia (p. 462) gives minute general directions for conducting alkaloidal assays and the monograph should be carefully read by all students. It divides alkaloidal assays into four groups:

Process A for Drugs, wherein an aliquot part of the extracted liquid is used in the assay.

Process B for Drugs, wherein the drug is totally extracted by percolation and the percolate thus obtained is used in the assay.

Process C for Galenicals, which is a method wherein an aliquot part of the extracted liquid is used.

Process D for Galenicals, which is a method wherein the total amount of extracted liquid is used. The monograph discusses the minutiæ of the assay, including extraction of the drug; shaking out with acid; shaking out with immiscible solvent; and finally stating that the extracted alkaloid is determined either volumetrically or gravimetrically. In the case of

Processes C and D careful directions are given as to the preparation of the sample, according to whether the product is a powdered extract, a pilular extract, a fluidextract or a tincture.

As typical examples, the official assays for cinchona and its preparation are given below:

Outline of Assay of Cinchona.—Digest 5 Gm. powdered cinchona with a mixture of hydrochloric acid and water, then add chloroform, ether and ammonia water and water. From this mixture decant the amount of clear fluid representing 4 Gm. drug. Filter into a separator and shake out with diluted sulfuric acid. Put the acid solution in another separator, make alkaline with ammonia water, shake out with chloroform, evaporate the chloroformic extracts and after purifying by dissolving in alcohol and again evaporating to dryness, at 100° C., weigh the alkaloidal residue. For details, see U.S.P., p. 122.

Outline of Assay of Compound Tincture of Cinchona.—Distribute 50 cc. of the tincture over asbestos fiber or paper pulp and after evaporating to dryness at 100° C. proceed to assay as in the case of cinchona. See U.S.P., p. 396.

From the above assays it is seen that the process of manipulation is tedious and intricate. It can be noted, however, that there are really three steps in the process: the *extraction* of the drug with ether and chloroform; the *shaking out*, first, with normal sulfuric acid and water, then (after rendering alkaline) with chloroform and lastly, evaporation of solution and *weighing* of alkaloids. The "*separator*" mentioned in the assay means one of the separatory funnels pictured on page 163.

Gravimetric alkaloidal assays are also provided in U.S.P. XI for the following drugs and preparations:

Colchicum seed
Tincture of colchicum seed
Cantharides

OFFICIAL ASSAYS IN WHICH THE ALKALOID IS TITRATED

As typical titration alkaloidal assays, the methods prescribed by U.S.P. XI for belladonna and its preparations are given below:

Outline of Assay of Belladonna Root.—Macerate 10 Gm. drug with 10 cc. of alcohol and 20 cc. of ether and 8 cc. ammonia water. Then percolate to exhaustion and transfer the entire percolate to a separator (p. 163), shake out with several portions of diluted sulfuric acid. Make the acid extract alkaline with ammonia water, shake out with several portions of chloroform, evaporate on a water bath, dissolve the residue in a known excess of $n/2$ H_2SO_4 and then titrate excess of acid with $n/50$ NaOH. Indicator, methyl red T.S. For details, see U.S.P., p. 85.

Outline of Assay of Fluidextract of Belladonna Root.—Mix 10 cc. of the fluidextract with an equal volume of water, make alkaline with ammonia, shake out with chloroform. Transfer the chloroformic layer to a separator (p. 163), shake out with several portions of diluted sulfuric acid and proceed as in the assay of belladonna root. For details, see U.S.P., p. 169.

The Assay of Belladonna Leaves is like that of belladonna root. For details, see U.S.P., p. 84.

Outline of Assay of Pilular Extract of Belladonna.—Dissolve 3 Gm. of extract in 10 cc. of chloroform. Add 10 cc. $n/10$ H_2SO_4 and 40 cc. of distilled water and evaporate on a water bath until the chloroform has evaporated. Then proceed as in the assay of belladonna root. For minor variations and other details, see U.S.P., p. 154.

The Assay of Powdered Extract of Belladonna is like that of pilular extract of belladonna. For minor variations and other details, see U.S.P., p. 155.

Outline of Assay of Tincture of Belladonna.—Evaporate 100 cc. of the tincture in a water bath to about 10 cc. and proceed as in the assay of fluidextract of belladonna root. For minor variations and other details, see U.S.P., p. 393.

Outline of Assay of Belladonna Plaster.—Extract 10 Gm. belladonna plaster in strips with chloroform, alcohol and some ammonia water. After the mass has separated from the cloth base, dry the cloth, weigh it and subtract its weight from the weight of the spread plaster. Then pour the chloroform-alcohol solution into a separator, mix with distilled water, draw off the chloroform layer, transfer it to another separator and rinse it out with more water. Combine with aqueous extracts, shake them out with more chloroform, which is to be mixed with the original chloroform extract. The mixed chloroform solution is then shaken out several times with weak sulfuric acid, the acid extracts are put with another separator, are made alkaline with ammonia water and are shaken out with chloroform. The filtered chloroform extracts are evaporated to dryness, the residue is dissolved in exactly 50 cc. of $n/50$ H_2SO_4, and the excess of acid is titrated with $n/50$ NaOH. Indicator, cochineal T.S. For details, see U.S.P., p. 140.

The following drugs and preparations are assayed by similar methods of titration:

Hyoscyamus
Extract of hyoscyamus
Tincture of hyoscyamus
Ipecac
Fluidextract of ipecac
Nux vomica
Extract of nux vomica
Tincture of nux vomica
Opium
Powdered opium
Granulated opium
Tincture of opium
Camphorated tincture of opium
Stramonium
Extract of stramonium (pilular and powdered)
Tincture of stramonium

For details, consult, the Pharmacopœia.

Volumetric assays are provided in U.S.P. XI for the following alkaloidal salts:

Codeine phosphate
Eucaine hydrochloride
Ephedrine sulfate
Ephedrine hydrochloride

For details, consult the Pharmacopœia.

"CASSIA FLASK" ASSAYS OF VOLATILE OILS

At this place, mention should be made of the assays of oils for phenols or for aldehydes based upon the formation of a water-soluble compound of these substances and the subsequent liberation of the free phenol or aldehyde and the direct reading of its volume in a "cassia flask." Four official oils are thus assayed—clove (p. 849); cinnamon (p. 845); chenopodium (p. 841); and spearmint (p. 848). On the pages just designated the Pharmacopœia assay for each oil is given in abstract.

Five official spirits—orange compound, lavender, peppermint, spearmint and anise—are assayed by "salting out" with calcium chloride solution and measuring the amount of separated oil in a "Babcock" bottle after centrifuging.

SAPONIFICATION NUMBER OF OILS AND FATS

As already explained on page 728, fixed oils and fats are esters of glycerin with fatty acids, and the process of soap making is the cooking of such oils with soda or potassa, whereby the sodium or potassium salts of the fatty acids are obtained. This fact is utilized in the assay of oils and fats, a given weight of the fatty substance being boiled with a known excess of alcoholic potassium hydroxide T.S. (p. 1008), and titrated with half-normal hydrochloric acid. In this way we can find out the exact amount of alkali taken up by the oil, and thus the "saponification number" can be deduced.

The pharmacopœial process may be outlined as follows:

Outline of the Estimation of the Saponification Value.—Accurately weigh 1.5 to 2.0 Gm. of the fat or oil, mix with 25 cc. of alcoholic $n/2$ KOH, and heat for thirty minutes on a water bath in a flask provided with an upright condensing tube. Then titrate with $n/2$ HCl using phenolphthalein T.S. as indicator. At the same time titrate 25 cc. of alcoholic $n/2$ KOH with $n/2$ HCl.

The difference between the number of cc. of $n/2$ HCl used by the straight alcoholic KOH, and by the same solution after treatment of the fat, multiplied by 28.06 and divided by the weight of the fat, gives the saponification value. For details, see U.S.P., p. 445.

The saponification number means the number of milligrams absolute potassium hydroxide which combines with 1 Gm. of oil. Thus, taking an example of calculating by process given above, suppose 2 Gm. of olive oil combines with 13.9 cc. half-normal potassium hydroxide V.S. That is, suppose it takes 25 cc. half-normal hydrochloric acid V.S. to neutralize 25 cc. alcoholic potassium hydroxide *before* saponification, and 11.1 cc. half-normal hydrochloric acid V.S. to neutralize the 25 cc. alcoholic potassium hydroxide *after* saponification. The calculations in this case would be 25 − 11.1 = 13.9,

$$\frac{13.9 \times 28.05}{2} = \frac{379.98}{2} = 189.99$$

and the saponification number is 189.99.

Now let us see the amount of potassa combining with the oil:

1 cc. $n/2$ KOH = 0.02805 Gm. absolute KOH (p. 1008).
13.9 cc. $n/2$ KOH = 13.9 × 0.02805 = 0.379898 Gm. absolute KOH.

Hence we see that 2 Gm. oil combines with 380 mg. KOH and 1 Gm. oil combines with 190 mg. KOH.

SAPONIFICATION NUMBER OF OFFICIAL OILS AND DRUGS

The following oils and fats are thus assayed:

	Sap. No		Sap. No.
Olive oil	190–195	*Oil of theobroma*	188–195
Expressed oil of almond	191–200	*Chaulmoogra oil*	196–213
Cottonseed oil	190–198	*Cod liver oil*	180–192
Linseed oil	187–195	*Lard*	195–203
Castor oil	179–185	*Suet*	193–200
Corn oil	188–193		

The manipulation employed in determining the saponification numbers of storax and balsam of tolu differs from the routine method; hence these are printed below:

Storax.—Accurately weigh about 2 Gm. purified storax, mix with 50 cc. of purified petroleum benzin, add 25 cc. alcoholic KOH V.S. and macerate twenty-four hours, with frequent shaking. Then titrate with $n/2$ HCl V.S. Indicator, phenolphthalein. Saponification number, 160 to 200. For details, see U.S.P., p. 364.

Balsam of Tolu.—Similar to storax. Saponification number, 154–220.

The assay of official waxes differs from the saponification number determination in the fact that both free acid and esters are determined in the same sample. The official directions are as follows:

Yellow Wax.—Accurately weigh about 3 Gm. wax, warm with 25 cc. neutral dehydrated alcohol until melted and titrate, while warm, with alcoholic KOH, using phenolphthalein as indicator. Acid value, 18 to 24. Then add another 25 cc. alcoholic KOH and some alcohol, boil for four hours in flask connected with reflux condenser and titrate excess of alkali with $n/2$ HCl. Ester value, 72 to 77. For details, see U.S.P., p. 114.

White Wax.—Proceed exactly as in the case of yellow wax. Acid value, 17 to 23. Ester value 72 to 79. For details, see U.S.P., p. 114.

The *ester assays* of volatile oils are modifications of the saponification number determination. Six volatile oils are thus assayed in the present Pharmacopœia.

Methyl Salicylate.—Accurately weigh about 2 cc. of the oil mix with 50 cc. alcoholic KOH, heat for two hours on a water bath, in a flask connected with reflux condenser, then titrate excess of alkali with n/2 HCl. Indicator, phenolphthalein T.S. For details, see U.S.P., p. 234.

Oil of Peppermint (ester assay).—Accurately weigh 10 cc. of the oil and boil with 25 cc. alcoholic KOH for one hour in a flask connected with a reflux condenser. After cooling, titrate the excess of alkali with n/2 H_2SO_4, using phenolphthalein as indicator. The number of cubic centimeters of alcoholic KOH consumed by the oil multiplied by 9.912 and divided by the weight of the oil, gives the percentage of menthyl acetate. For details, see U.S.P., p. 259.

Oil of Peppermint (menthol assay).—Acetylize 10 cc. of the oil by heating in an acetylization flask with acetic anhydride and anhydrous sodium acetate for one hour. Cool, and then wash, dry and accurately weigh about 5 cc. of acetylized oil. Then boil the acetylized oil for one hour with 50 cc. n/2 alcoholic KOH, in a flask connected with a reflux condenser. After cooling, titrate excess of alkali with n/2 H_2SO_4, using phenolphthalein T.S. as indicator. For the menthol calculation and other details, see U.S.P., p. 259.

Oil of Rosemary (ester and borneol assays). Exactly like the ester and menthol assays of oil of peppermint except that the factor is different. For details, see U.S.P., p. 267.

It will be noticed that there are 2 parts to the assay of oils of peppermint and oil of rosemary: The first part resembling a saponification number determination, while the second part—a phenol assay—depends upon the acetylization of that substance.

As to the saponification tests, it will be seen that the factors (9.912 for the menthyl acetate of oil of peppermint; 9.811 for the bornyl acetate of oil of rosemary) represent the molecular weight of the characteristic ester divided by 200, or 100 times the amount of ester that combines with 1 cc. half-normal potassium hydroxide V.S.

This can best be explained by a hypothetic assay.

Suppose we find 9 Gm. of oil of peppermint combine with 7.5 cc. half-normal alcoholic KOH; that is, while the 25 cc. half-normal alcoholic KOH took 25 cc. half-normal H_2SO_4 *before* saponification, after saponification the alkali left took only 17.5 cc. half-normal H_2SO_4. In such cases we find—

that (*a*) 9 Gm. oil = 7.5 cc. n/2 alcoholic KOH
that (*b*) 1 cc. n/2 alcoholic KOH = 0.09912 Gm. menthyl acetate
that (*c*) 7.5 cc. n/2 alcoholic KOH = 7.5 × 0.09912
= 0.7434 Gm. menthyl acetate
Therefore that (*d*) 9 Gm. oil = 0.7434 Gm. menthyl acetate
and that (*e*) 9 Gm. oil $= \frac{100}{9} \times 0.7434 = 8.26$ per cent menthyl acetate.

Careful examination of the above figures shows that the real calculation "*c*" and "*e*" means the multiplication of the number of cubic centimeters of alcoholic potassa used by 0.09912 and by 100 (or by 9.912), and finally dividing by weight of oil. In passing, it may be stated that the use of the acetylization factors (7.808) for the menthol in oil of peppermint and 7.710 for the borneol in oil of rosemary) can be explained in the same way.

Oil of Pine Needles.—Ester assay exactly like that directed for oils of lavender and peppermint, starting with 10 cc. of the oil and using as factor, 9.811.

Oil of Santal.—Assay for the alcohol, santalol, exactly as directed in the menthol assay of oil of peppermint except that the factor is different. For details, see U.S.P., p. 267.

It will be noticed that in examining these six oils, two types of assays are provided. One of these (the ester assay) resembles the saponification number determination; the other (the alcohol assay) depends upon the acetylization of that substance.

Oil of Lavender.—Accurately weigh about 5 cc. of the oil and boil with 50 cc. alcoholic KOH for one hour in a flask connected with a reflux condenser. After cooling titrate the excess of alkali with $n/2$ H_2SO_4, using phenolphthalein as indicator. The number of cubic centimeters of alcoholic KOH consumed by the oil multiplied by 9.811 and divided by weight of oil taken gives percentage of linalyl acetate. For details, see U.S.P., p. 257.

The *acetylization tests* given above for oil of peppermint and for oil of rosemary, as well as that for the santalol in oil of santal, given below, are based on the fact that the characteristic alcohols of these three oils form well-defined acetyl compounds when boiled with acetic acid anhydride and sodium acetate, in the appropriate "acetylization flask" (Fig. 277); that this oil, separated from the aqueous liquid, washed with water, and dried, can be saponified like any other ester, and from the amount of alcoholic potassa required for saponification the amount of alcohol can be estimated.

THE ACID NUMBER OF RESINS

As mentioned on page 872, true resins contain resin acids. These resin acids, like other acids, combine with alkali in molecular proportions. Hence their amount can be estimated by titration with volumetric alkali solution. The pharmacopœial directions for acid number estimations may be summarized as follows:

Acid Number for Resins.—This represents the number of milligrams of potassium hydroxide required to neutralize 1 Gm. of resin. Accurately weigh about 2 Gm resin, dissolve it in alcohol and titrate with $n/2$ NaOH, using phenolphthalein as indicator. Each cubic centimeter of half-normal alkali used, multiplied by 0.02805 and divided by the weight of the resin equals the acid number. For details, see U.S.P., p. 444.

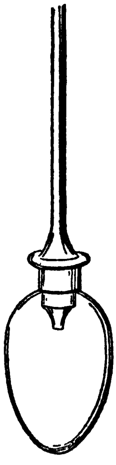


Fig. 277.—Acetylization flask.

The official substances so tested are:

	Acid Number
Rosin	Not less than 150
Storax	38 to 85
Balsam of Tolu	112 to 168
Balsam of Peru	56 to 84
Copaiba	28 to 95

The manipulation of the last 3 cases is quite complex. For details see U.S.P.

IODINE ABSORPTION NUMBER

As already explained on page 663, fixed oils, like all other unsaturated bodies, when treated with halogens, notably iodine, loosen whatever double bonds they possess, attaching an atom of the halogen to each bond thus freed; hence each double bond in such oil takes up 2 atoms of iodine. As the percentage of unsaturated ester differs in each fixed oil, the different fixed oils absorb different amounts of iodine; hence the iodine absorption number is a valuable aid to identification and differentiation of oils.

The Pharmacopœia gives a monograph on the subject that may be summarized as follows:

Accurately weigh about 0.8 Gm. solid fat or 0.3 Gm. oil (exceptions linseed, cod liver and theobroma oils), dissolve it in chloroform and add to the solution iodobromide test solution U.S.P. Macerate one-half hour (longer with castor and linseed oils) being sure that at the end of the maceration, the mixture is colored brown by free iodine. Then add potassium iodide and distilled water and titrate the excess of iodine with

$n/10$ sodium thiosulfate, using starch paste as indicator. Run a blank test of the iodo-bromide T.S. with the thiosulfate V.S. and the difference between the cubic centimeters of $n/10$ $Na_2S_2O_3$, used by the straight iodo-bromide solution and the number of cubic centimeters used by the same solution after treatment with fat, multiplied by 1.269 and divided by the weight of the fat, gives the iodine value of the fat. The iodo-bromide solution is made by dissolving iodine in glacial acetic acid and then adding bromine to the solution. For details, see U.S.P., p. 445.

Explaining the arithmetic of this process, let us suppose that 0.3 Gm. of a certain fat plus 25 cc. iodo-bromide T.S. takes 60 cc. tenth-normal thiosulfate V.S. to decolorize, while in the blank experiment 25 cc. iodo-bromide T.S. take 90 cc. tenth-normal thiosulfate V.S. for decolorization. This would mean that 0.3 Gm. fat absorbed 90 − 60, or 30 cc. tenth-normal thiosulfate V.S.

1 cc. $n/10$ thiosulfate V.S. = 0.01269 Gm. iodine (p. 1011).
30 cc. $n/10$ thiosulfate V.S. = 30 × 0.01269 Gm. iodine.
= 0.3807 Gm. iodine.
Hence 0.3 Gm. fat absorbed 0.3807 Gm. iodine.
Hence 100 Gm. fat would absorb $\frac{1000}{3} \times 0.3807$ Gm. iodine.
or 126.9 Gm. iodine.

The factor as given in the Pharmacopœia is: subtract from amount thiosulfate V.S. consumed in blank test (in our case, 90 cc.) the amount consumed in actual test (in our case, 60 cc.) and the difference (30, in our case) multiplied by 1.269 and divided by weight of fat taken (in our case 0.3 Gm.) gives the iodine value

$$\frac{30 \times 1.269}{0.3} = 126.9$$

which shows that the so-called "iodine number" means *the number of grams of iodine absorbed by 100 Gm. of fat.*

The following official oils are tested exactly as in the process given above:

	Iodine value		Iodine value
Castor Oil	83– 88	Oil of Theobroma	35–40
Chaulmoogra Oil	93–104	Lard	46–70
Cod Liver Oil	145–180	Suet	33–48
Cotton Seed Oil	105–114	Wool Fat	18–36
Expressed Oil of Almond	93–110	Soap (Acids from)	83–92
Linseed Oil	at least 170		
Olive Oil	79– 88		
Corn Oil	112–128		

SPECIAL ORGANIC VOLUMETRIC ASSAYS

I. PHENOL ASSAY WITH KOPPESCHAAR'S SOLUTION

As the theory of this assay is given on page 772, it is merely necessary to insert pharmacopœial directions and to calculate results:

TENTH-NORMAL BROMINE VOLUMETRIC SOLUTION

[KOPPESCHAAR'S SOLUTION]

Br = 79.92 7.992 Gm. in 1000 cc.

Condensed Recipe.

Dissolve 3 Gm. potassium bromate and 25 Gm. potassium bromide in enough water to make 1000 cc. Standardize 25 cc. of this by treatment with hydrochloric acid and potassium iodide and then titrate the liberated iodine with $n/10$ sodium thiosulfate. Then dilute the bromine solution so that each cubic centimeter corresponds to 1 cc. $n/10$ $Na_2S_2O_3$. For details, see U.S.P., p. 565.

The Pharmacopœia gives the equivalent factor for two chemicals assayed with tenth-normal bromine; phenol and resorcinol.

As a typical assay of this character the titration of phenol is given below:

Phenol.—Treat a known quantity of an aqueous solution of phenol (containing between 0.038 and 0.041 Gm. C_6H_5OH) with 30 cc. of $n/10$ bromine, add hydrochloric acid and potassium iodide solution, then add a little chloroform and titrate with $n/10$ sodium thiosulfate. From amount of $n/10$ $Na_2S_2O_3$ used, calculate amount of $n/10$ Br used by the phenol. For details, see U.S.P., p. 285.

It will be seen that a certain amount of bromine is absorbed by the phenol; that the excess liberates iodine from the added potassium iodide, and that the iodine thus freed is titrated with tenth-normal thiosulfate solution.

We have already learned (p. 1011) that 1 cc. tenth-normal thiosulfate V.S. equals 1 cc. tenth-normal iodine V.S., and as the bromine liberates iodine atom for atom, 1 cc. tenth-normal thiosulfate solution must equal 1 cc. tenth-normal bromine solution.

We find above that 1 cc. $n/10$ bromine V.S. = 0.001568 Gm. phenol. This is because the reaction between bromine and phenol runs as follows:

$$\begin{array}{lcl} C_6H_5OH & + \; 6Br & = C_6H_2Br_3OH + 3HBr. \\ 94.05 & 6 \times 79.92 & \\ & \text{or } 479.52 & \end{array}$$

We therefore see—

$$\begin{array}{rcl} 479.52 \text{ Gm. Br} & & = 94.05 \text{ Gm. } C_6H_5OH. \\ \text{Hence } 79.92 \text{ Gm. Br} & = \frac{94.05}{6} & = 15.68 \text{ Gm. } C_6H_5OH. \\ \left.\begin{array}{r}\text{and } 7.992 \text{ Gm. Br} \\ \text{or } 1000 \text{ cc. } n/10 \text{ Br}\end{array}\right\} & & = 1.568 \text{ Gm. } C_6H_5OH. \\ \text{Hence } 1 \text{ cc. } n/10 \text{ Br} & & = 0.001568 \text{ Gm. } C_6H_5OH. \end{array}$$

In the pharmacopœial assay of phenol we take a solution equivalent to about 0.04 Gm. phenol, mix it with 30 cc. tenth-normal bromine V.S., then with acid and potassium iodide, and finally titrate the freed iodine with tenth-normal thiosulfate V.S. Suppose it takes 6 cc. thiosulfate solution to decolorize, that would mean that there had been in the solution before adding the potassium iodide 6 cc. tenth-normal bromine and that the phenol had combined with 30 − 6 or 24 cc. tenth-normal bromine.

Since 1 cc. $n/10$ Br V.S. = 0.001568 Gm. phenol.
24 cc. $n/10$ Br V.S. = 24 × 0.001568 Gm. phenol.

Hence 0.04 Gm. of the sample of phenol contained 0.037632 Gm. absolute phenol or $\frac{37,632}{40,000}$ of 100 per cent or 94 per cent absolute phenol.

For other official assays of this character, consult the monographs for *liquefied phenol*, ointment of phenol and resorcinol as given in U.S.P. XI.

II. SUGAR ASSAY WITH FEHLING'S SOLUTION

This assay has been discussed on page 695, and as neither of the official sugars is directed to be assayed, we can leave the subject after presenting an outline of the pharmacopœial directions and a few additional remarks.

ALKALINE CUPRIC TARTRATE VOLUMETRIC SOLUTION

[Fehling's Solution]

Condensed Recipe.

Two solutions are prepared.

Solution A consists of 34.66 Gm. uneffloresced copper sulfate U.S.P. dissolved in enough distilled water to make 500 cc.

Solution B is made by dissolving 173 Gm. crystalline potassium and sodium tartrate U.S.P. and 50 Gm. sodium hydroxide U.S.P. in enough distilled water to make 500 cc. Mix equal volumes of the two solutions at the time of titration. U.S.P. IX gave directions for keeping these solutions and also the equivalent factors for carbohydrates. Each cubic centimeter of the mixed solution represents 0.00500 Gm. anhydrous glucose (dextrose); 0.00475 Gm. cane sugar (sucrose), after inversion; and 0.00678 Gm. anhydrous milk sugar (lactose). U.S.P. XI (p. 549) omits these data and emphasizes that the solution is used pharmacopoeially only as a qualitative test solution.

It will be seen from the above that 10 cc. of mixed solution equals 5 cg. (0.05 Gm.) of glucose (dextrose). In carrying out the assay, the mixed solution (10 cc.) is put into an evaporating dish, is diluted with water (say 50 cc.), and is brought to the boiling point.

The diluted sugar solution (usually diabetic urine, as far as the pharmacist is concerned) is put into a burette and is dropped into the boiling solution, little by little, until all the copper is precipitated. Details are beyond the scope of this work; hence the reader is referred to some standard book on urinary analysis mentioned in the Preface.

The process outlined above involves a peculiar form of calculation; for we see that in this case, contrary to the usual assay, the volumetric solution is measured and the liquid whose strength is to be determined is dropped from the burette. This makes our report read something like this: 10 cc. Fehling's solution are completely precipitated by 15 cc. of urine. In such case the calculation runs as follows:

10 cc. Fehling's solution = 15 cc. urine.
10 cc. Fehling's solution = 0.05 Gm. glucose.
Hence 15 cc. urine contained 0.05 Gm. glucose.
Hence 100 cc. urine contained $\frac{100}{15} \times 0.05$ or 0.333 Gm. glucose.

and we ordinarily say that such urine contains 0.333 per cent ($\frac{1}{3}$ of 1 per cent) glucose, although bear in mind that in exact chemical operations percentage should mean grams to 100 Gm., and not grams to 100 cc.

Before leaving this topic mention should be made of the large number of modifications of the original solution, such as Pavy's, Purdy's, Haines' and Benedict's solutions. All of these are copper solutions designed for preservation in mixed form and intended to give a sharper end point.

CHAPTER LVII

GRAVIMETRIC, GASOMETRIC AND OTHER ASSAYS

Gravimetric analysis, as explained on page 995, is the determination of the quantity of a certain ingredient of a given substance by the separation of this ingredient, free, in combination, or possibly in reduced form, weighing the solid so separated, and from the weight obtained deducing the amount in the original compound.

Ordinarily, the process consists of precipitating the ingredient as an insoluble compound, but in the final grouping this class of analysis includes such assays as the extracting and weighing of alkaloids (see Cinchona Assay, p. 1021), the burning of organic salts to carbonates, which are then weighed, and the separation of a button of metal from the ore in the so-called "fire assays."

The pharmacopœial gravimetric assays may be grouped into (*a*) precipitation assays; (*b*) incineration of metallic compounds and weighing the resulting oxide.

PRECIPITATION ASSAYS

These are conducted by taking an aqueous solution of a soluble salt, adding thereto the appropriate precipitant (p. 165), collecting the insoluble form of the desired ingredient thus precipitated, and weighing same after carefully washing it free from soluble impurity and after heating until all moisture and volatile impurities are driven off. The process can best be explained by a few typical examples.

We want to estimate the amount of sulfate in a certain batch of dried sodium sulfate. We take 0.2 Gm. of the sulfate, dissolve in water and add barium chloride T.S., when the following reaction occurs:

(*a*) $Na_2SO_4 + BaCl_2 = 2NaCl + BaSO_4$.
142 06 208.27 2 × 58.46 233.43

The insoluble barium sulfate is collected on a filter, washed, dried, and weighed, when we find in the case under consideration that 0.2 Gm. Na_2SO_4 gave 0.325 Gm. $BaSO_4$.

From the equation above we find:

0.233 Gm. $BaSO_4$ = 0.142 Gm. absolute Na_2SO_4.
Then 0.325 Gm. $BaSO_4$ = $^{325}/_{233} \times 0.142 = 0.197$ Gm. absolute Na_2SO_4.

Hence we see that the 0.2 Gm. sodium sulfate contained 0.197 Gm. absolute Na_2SO_4.

If it is desired to determine only the acidulous portion (SO_4) of the sodium sulfate, the calculation runs like this:

$Na_2SO_4 + BaCl_2 = 2NaCl + BaSO_4$.
46 + 96.05 208.27 2 × 58.45 233.42
142.05
0.233 Gm. $BaSO_4$ = 0.096 Gm. SO_4.
Then 0.325 Gm. $BaSO_4$ = $^{325}/_{238} \times 0\ 096 = 0.133$ Gm. SO_4.
We therefore see that
0.2 Gm. Na_2SO_4 contained 0.133 Gm. SO_4,
or $^{133}/_{200} \times 100 = 66.5$ per cent SO_4.

Another case, showing that the process is applicable to the determination of the basic constituent of a salt as well as the acidulous portion, might be given. Two-tenths Gm. silver nitrate is precipitated by hydrochloric acid as silver chloride, as shown in the following equation:

$AgNO_3 + HCl = AgCl + HNO_3$.
169.89 36.47 143.34 63.02

We find in the assay that 0.2 Gm. silver nitrate gives 0.165 Gm. dried silver chloride.

From the equation above we find that—

0.143 Gm. AgCl = 0.169 Gm. absolute $AgNO_3$.
Then 0.165 Gm. AgCl = $^{165}/_{143} \times 0.169 = 0.195$ Gm. absolute $AgNO_3$.
Hence 0.200 Gm. of the silver nitrate contained 0.195 Gm. absolute $AgNO_3$ or $^{195}/_{200} \times 100$ per cent, or 97.5 per cent absolute $AgNO_3$.

Expressed as quantity of metallic silver, the calculation runs like this:

$$\underbrace{\underset{107.88}{Ag}\quad\underset{62.01}{NO_3}}_{169.89} + \underset{36.47}{HCl} = \underset{143.34}{AgCl} + \underset{63.02}{HNO_3}.$$

0.143 Gm. AgCl = 0.108 Gm. metallic silver,

Then 0.165 Gm. AgCl = $^{165}/_{143} \times 108$ = 0.124 Gm. metallic silver.

Hence 0.200 Gm. of the silver nitrate contains 0.214 Gm. metallic silver, or $^{124}/_{200} \times 100$ per cent = 62 per cent metallic silver.

The above sketchy outline gives but a glimpse of the important and difficult branch, gravimetric analysis, and for details of the work the reader is referred to such standard works on the subject as Treadwell and Hall or Fresenius. Before dismissing the subject, the statement should be made that in gravimetric calculations exact molecular weights should be used; that weights and calculations should be carried to the fourth decimal place, and that because of the extreme skill and the amount of time required to obtain accurate results, the process is not largely used in pharmacopœial assays.

The precipitation assays of the present Pharmacopœia can be grouped as follows:

1. Precipitation as barium sulfate and weighing as such.
2. Precipitation as magnesium phosphate and weighing as magnesium pyrophosphate.
3. Precipitation as aluminum hydroxide and weighing as aluminum oxide.
4. Precipitation as zinc sulfide and weighing as zinc oxide.
5. Precipitation as mercuric sulfide and weighing as such.

BARIUM SULFATE ASSAYS

This type of assay has been explained on page 997, so we can proceed to the study of pharmacopœial directions.

Sodium Sulfate.—Accurately weigh about 1 Gm. sodium sulfate, dissolve in distilled water, acidulate with hydrochloric acid, heat to boiling and then precipitate by adding an excess of hot barium chloride T.S., heat mixture thirty minutes on a water bath, then collect the $BaSO_4$ on a filter, wash until free from chlorides, then ignite and weigh. For details, see U.S.P., p. 349.

Sublimed Sulfur.—Accurately weigh about 1 Gm. well-dried sulfur, mix with 50 cc. of 10 per cent potassium hydroxide solution and boil until a clear golden-yellow liquid results. Dilute this with distilled water and then oxidize one tenth of it with solution of hydrogen dioxide. Acidulate the resulting solution of sodium sulfate with hydrochloric acid, dilute it with water, heat to boiling, add hot barium chloride T.S. and then heat the mixture on a water bath for thirty minutes. Collect the precipitate of barium sulfate, wash, dry, ignite and weigh it. Also run a blank test and if any barium sulfate precipitate occurs, weigh it and deduct from the weight of barium sulfate obtained in the real assay. For details, see U.S.P., p. 368.

In this assay, the sulfur is made soluble by boiling with alkali (p. 429), the resulting potassium sulfide is oxidized with hydrogen dioxide to the sulfate which is then precipitated with barium chloride.

Washed Sulfur and *Precipitated Sulfur* are assayed in the same manner.

MAGNESIUM PHOSPHATE ASSAYS

These are based upon the fact that when a magnesium salt is treated with sodium phosphate in alkaline (ammoniacal) solution, ammonio-magnesium phosphate precipitates (p. 999). This magnesium phosphate upon heating is converted into the pyrophosphate, which is weighed.

Magnesium Sulfate.—Accurately weigh about 1 Gm. magnesium sulfate, dissolve it in water, add to the solution sodium phosphate T.S. and then ammonia water and let mixture stand for four hours. Collect the precipitate on a filter, wash it with a diluted ammonia water until free from sulfate, then dry and ignite. For details, see U.S.P., p. 227.

Methods similar to this are employed in the assays of:

Sodium phosphate
Exsiccated sodium phosphate
Solution of magnesium citrate

For details, consult U.S.P. XI.

ALUMINUM HYDROXIDE ASSAYS

In these, a solution of the aluminum salt is treated with ammonium hydroxide, usually after the addition of a solution of ammonium chloride. The precipitate of aluminum hydroxide (p. 1000) thus produced is heated, when the oxide, Al_2O_3, is obtained.

Alum.—Accurately weigh about 1 Gm. alum, dissolve it along with 1 Gm. ammonium chloride in distilled water, boil and add a slight excess of ammonia water. Collect the precipitate, wash with hot distilled water, dry, ignite and weigh as Al_2O_3. For details, see U.S.P., p. 50.

Exsiccated Alum.—Like alum, except that about 0.5 Gm. of salt is taken.

ZINC SULFIDE ASSAYS

When zinc salts are treated with ammonium sulfide in alkaline solution, a white precipitate of zinc sulfide (p. 1000) results. When this is heated, zinc oxide is produced.

Zinc Acetate.—Accurately weigh about 1 Gm. zinc acetate, dissolve in distilled water, add ammonia water to faint alkalinity, warm to 90° C. and then add ammonium sulfide T.S. and warm on a water bath. Collect the precipitate, wash with distilled water containing a trace of ammonium sulfide, then dissolve in hot 20 per cent nitric acid, evaporate, ignite and weigh as zinc oxide. For details, see U.S.P., p. 431.

This method is also employed in the assays of *zinc chloride*, *zinc sulfate*, and ointment of *zinc oxide*. For details, consult the Pharmacopœia.

MERCURY ASSAYS

Corrosive Mercuric Chloride.—Accurately weigh about 0.5 Gm. well-dried chloride, dissolve in distilled water containing a little hydrochloric acid and then saturate the solution with hydrogen sulfide gas. Collect the precipitated mercuric sulfide on counterpoised filters, wash with water, then with alcohol, then with carbon tetrachloride, and again with alcohol. Dry at 110° C. and weigh. For details, see U.S.P., p. 186.

This method is also employed in the assays of *ammoniated mercury*, *ointment of mercuric oxide* and *poison tablets of mercury bichloride.* For details consult the Pharmacopœia.

BISMUTH ASSAYS

Bismuth and Potassium Tartrate.—Dissolve 0.4 Gm. of the salt in 100 cc. of distilled water, acidulate with hydrochloric acid, warm and pass hydrogen sulfide through the liquid. Collect the precipitate of bismuth sulfide in a Gooch crucible, wash, dry and weigh. For details, see U.S.P., p. 88.

IGNITION ASSAYS

These are carried out by heating the compound (frequently a salt of an organic acid) until nothing remains except the metallic oxide, which is then weighed.

Bismuth Subcarbonate.—Accurately weigh about 1 Gm. of the salt, ignite at red heat and weigh the resulting bismuth oxide. For details, see U.S.P., p. 89.

The following compounds are assayed by similar ignition methods:

Bismuth subgallate
Bismuth subnitrate
Bismuth subsalicylate
Calcium creosotate
Tincture of iodine (for KI)
Mild tincture of iodine (for NaI)

GRAVIMETRIC ORGANIC ASSAYS

Before closing the subject of gravimetric assays attention must be called to the six assays in which the alkaloids or other active principles are extracted from salts by the "shaking out" process and then weighed. A typical one is the following:

Caffeine Citrate.—Weigh accurately about 0.5 Gm. of the citrate, dissolve in 10 cc. of hot water, add sodium hydroxide T.S., pour into a separator and then shake out with three portions of chloroform. Evaporate the chloroformic extract to dryness and then weigh. For details, see U.S.P., p. 94.

Similar gravimetric assays are provided by U.S.P. XI for the following:

Caffeine sodio-benzoate
Quinine and urea hydrochloride
Theobromine sodio-salicylate
Theophylline with ethylene diamine
Theophylline with sodium acetate
Ethyl hydrocupreine
Diluted erythrol tetranitrate

For details, consult the Pharmacopœia.

Other gravimetric organic assays are the pyroxylin assay given under collodion; the filicin assay given under oleoresin of aspidium and the storax and balsam of Peru assays given below:

Storax.—Boil 2 Gm. of storax with 25 cc. $n/2$ alcoholic KOH under a reflux condenser for one hour. Neutralize with $n/2$ H_2SO_4; evaporate the alcohol, dissolve residue in water; shake out with ether to remove impurities; acidulate the aqueous layer with diluted sulfuric acid; and then shake out with four portions of ether. Recover the ether from the ethereal extract by distillation; boil the residue with water under a reflux condenser for fifteen minutes; and filter, while hot. Collect the separated crystals of cinnamic acid on a Gooch crucible, wash them with ice-cold water, dry and weigh. Storax should yield at least 25 per cent of cinnamic acid. For details, see U.S.P., p. 364.

Balsam Peru.—Accurately weigh 3 Gm. of the balsam, mix with 30 cc. sodium hydroxide T.S. in a separator (p. 163), shake with 60 cc. ether, separate the ethereal layer and evaporate 50 cc. of it. Weigh residue as cinnamein. Cinnamein content, 50 to 60 per cent. For details, see U.S.P., p. 79.

Lastly U.S.P. XI provides a gravimetric assay for *spirit of camphor* involving the formation of a precipitate, when the spirit is treated with dinitrophenyl hydrazine T.S. This precipitate is collected on a Gooch crucible, is washed, dried, and weighed. For details, see U.S.P., p. 353.

ANALYSIS OF VEGETABLE DRUGS

The Pharmacopœia provides for an elaborate examination of vegetable drugs from the chemical standpoint. The monograph describing the procedure should be read by the student. Among the items considered, the following may be summarized as follows:

Total Ash.—A maximum amount of ash is set for a number of official drugs as a study of the rubrics given on the preceding pages will show. Details as to ashing are given on page 473 of the Pharmacopœia.

Acid-insoluble Ash.—Not only is the amount of total ash of importance in establishing purity, but also in certain cases whether the ash is wholly soluble in diluted hydrochloric acid or only partially soluble. Details of manipulation are given on page 473 of the Pharmacopœia.

Volatile and Nonvolatile Ether-soluble Extractive.—In the case of spices and other drugs containing fatty matter, the amount of extract obtained by extracting with dehydrated ether is of great importance. The pharmacopœial procedure may be condensed as follows:

Determination of Volatile Extractive.—Extract 2 Gm. drug with anhydrous ether in a continuous extraction (Soxhlet) apparatus. Dry over sulfuric acid and weigh. This gives the total ether extract. Then heat the residue to constant weight at 110° C. The loss in weight represents the ether-soluble volatile extractive; the weight after heating at 110° C. is nonvolatile ether-soluble extractive. For details, see U.S.P., p. 475.

The official drugs thus tested are:

Drug.	Volatile ether-soluble extract.	Nonvolatile ether-soluble extract.
Capsicum	....	12 per cent
Cinnamon	2 per cent	
Clove	15 per cent	
Myristica	...	25 per cent

A modified type of this assay is found in *Linseed* (30 per cent of nonvolatile ether soluble extract of which 98 per cent must be saponifiable).

Alcohol-soluble Extractive.—The pharmacopœial assay may be condensed as follows: Place about 2 Gm. of drug in a suitable extraction apparatus (p. 185) and extract with alcohol during five hours. Dry the insoluble residue at 100° C. for thirty minutes and then weigh. For further details, see U.S.P., p. 475.

The following drugs are thus assayed:

Drug.	Alcohol-soluble extractive.
Benzoin (Sumatra)	75 per cent
Benzoin (Siam)	90 per cent
Kino	45 per cent
Myrrh	30 per cent

In one case; the factor given is based upon *solubility in diluted alcohol*; *Rhubarb* yielding 30 per cent of diluted alcohol-soluble extractive.

Water-soluble Extractive.—In these cases the drug is extracted with distilled water, the procedure resembling the determination of the alcohol-soluble extractive described above. The pharmacopœial drugs thus assayed are:

Drug.	Water-soluble extractive.
Gentian	30 per cent
Kino	80 per cent

GASOMETRIC ANALYSIS

This form of analysis is performed by liberating certain gases from appropriate substances by chemical action, measuring amount of gas obtained in a nitrometer or other measuring tube for gases; from the volume of the gas calculate its weight, and from its weight calculate the amount of chemical from which the gas was liberated. Two chemicals—spirit of ethyl nitrite and amyl nitrite—were assayed by this process in U.S.P. X, but in the new Pharmacopœia, these officials are assayed by a volumetric method. (See p. 1014.)

OTHER TYPES OF ASSAYS

Hydrogen-ion Concentration Determinations.—On page 407 it was stated that the hydrogen ionization of pure water is only 1 in 10,000,000. This latter figure is expressed by mathematicians as 10^7 (ten to its seventh power). The hydrogen-ion concentration of water or of acids is expressed mathematically by physical chemists in such means. Reversing the statement given above, in water only one-ten millionth (decimally 0.0000001) of the molecules are ionized and the decimal just given is expressed by mathematicians as 10^{-7}. This figure (10^{-7}) applies not only to water but to any acid or base in which the ionization was only 1 molecule in ten million, and such a condition is now expressed in chemistry by the symbol *p*H 7. This condition however is one of neutrality and the hydrogen-ion-concentration of acids is expressed as ranging from *p*H (1.008 Gm. of hydrogen ions in 10 liters of solution) to *p*H 6 (1.008 Gm. of hydrogen ions in 1 million liters of solution).

There is a marked distinction between the strength of a volumetric solution and of the hydrogen-ion concentration of the same solution. Thus, the strength of a volumetric solution is expressed as a definite number of grams of *atomic* hydrogen in a given volume of solution, whereas the hydrogen-ion concentration tells us the number of grams of *ionized* hydrogen in a given volume of solution. As stated above, it is entirely possible that in a certain dilution of a certain acid, only one-tenth of the hydrogen atoms are ionized; hence the *p*H of that acid would be much smaller than the *p*H of a more easily ionized acid.

The determination of the *p*H of a substance is now accomplished either by special volumetric or electrometric methods; methods which give far more accurate results than does ordinary volumetric procedure. Its employment is of distinct service in delicate chemical and pharmaceutical operations. (See p. 626.)

Colorimetric Assays.—In those cases where the quantity of substance is too small to determine either gravimetrically or volumetrically recourse is had to the fact that the intensity of a color reaction is proportional to the amount of the chemical present. Thus on page 501 it was stated that Nessler's reagent was used to determine minute amounts of ammonia present in water. Space prevents extended description of this method of assay and the reader is referred to the articles by the author and his coworkers on the subject given in the Bibliography at the end of this Chapter.

In U.S.P. X, the only colorimetric assay given was one for detecting free salicylic acid in acetylsalicylic acid. U.S.P. IX prescribed a colorimetric assay for dried suprarenals, comparing the color produced by treating the glands with manganese dioxide and water against the color of mixtures of gold chloride T.S. and cobaltous chloride T.S.

In U.S.P. XI the colors of several of the fixed oils are standardized by the Arny "Co-Fe-Cu" colored fluids and the same fluids are used in order to accurately determine the "readily carbonizable substances" test of a number of organic compounds. For details as to the "Co-Fe-Cu" fluids consult the papers mentioned in the Bibliography found at the end of this Chapter.

Electrolytic Assays.—On page 389 it was stated that when a current of electricity was passed through a solution of certain metallic salts, dissociation took place and the metallic ions migrate toward the negative pole where they lose their electric charge and deposit as the metal. If the proper conditions of temperature, time, strength of solution and of current are observed the metal deposits quantitatively and from its weight can be deduced the quality of the salt. U.S.P. X permitted, as optional methods, the electrolytic assays of copper, mercury, silver, and zinc salts, but the methods are not recognized in U.S.P. XI.

Polariscopic Assays.—We have already learned (p. 831) that the purity of many organic substances may be determined by determination of their optical rotation. To this fact we must now add the statement that the rotation of a solution of an optically active substance—say, sugar or camphor—is directly proportional to the strength of the solution. Thus the polariscope is not only of service in detecting impurities, but it can also be used in assaying the strength of preparations containing optically active chemicals. U.S.P. XI directs the use of the polariscope for identifying camphor, sucrose (sugar), lactose (milk sugar) and practically all of the volatile oils. In the Appendix to U.S.P. XI (pp. 459–461) the general subject of optical rotation is given due attention.

Biological Assays.—On page 720 an outline of the principles of biological or physiological assays was given. Here it will be merely mentioned that in the present Pharmacopœia such assays are compulsory for *aconite, digitalis, ergot, pituitary,* and their preparations and for *solution of epinephrine* and *solution of parathyroid;* while the vitamin content of *cod liver oil* and of *solution of irradiated ergosterol* is established biologically.

BIBLIOGRAPHY

Volumetric Assays—(Fehling's solution) Pellet, C.A., 9, 1916, 1699; Pégurier, Jl. Soc. Ch. Ind., 44, 1925, 1004B; Cattelain, C.A., 24, 1930, 3193; Morton, Quart. Jl. Ph., 4, 1931, 161; Dumanskii and Dikanova, C.A., 26, 1932, 1845. (Benedict's Solution) Haskins, C.A., 13, 1919, 850; Ionescu and Spirescu, C.A., 19, 1925, 1237. (Haine's Solution) Merck's Rept., 29, 1920, 60. (Ferrous assay) Marguerette, Am. chim. phys., [3], 18, 1846, 244. (Mercury assay) LaWall, Jl. A.Ph.A., 3, 1914, 50. (Boric Assay) Rimbach and Ley, C A , 16, 1922, 2056; Dubrisay, C.A., 15, 1921, 3953.

Biologic Assays.—Wood, A J P., 82, 1910, 101; Githens and Vanderkleed, *ibid.*, 82, 1910, 453; Hale, A.J P., 83, 1911, 97; Anon., Bull. A.Ph.A., 6, 1911, 22; Hamilton, Jl. A.Ph.A., 8, 1919, 49.

Hydrogen-ion Determinations.—Clark and Lubs, Jl. Bacteriol., 2, 1917, 1, 109 and 191; Schmidt and Hoagland, Univ. Cal. Pub. Physiol., 2, 1919, 23; McGill, Jl. A.Ph.A., 11, 1922, 1003 and 12, 1923, 853; Stroup, A.J.P., 92, 1920, 81 and Proc. P.P.A., 45, 1922, 243; Wherry and Adams, C.A., 15, 1921, 2763; Clark, C.A., 15, 1921, 2763; Leffmann, Jl. Frank. Inst., 197, 1924, 741; Moerck, Proc. P.P.A., 47, 1924, 201; Little, Jl. A.Ph.A., 15, 1926, 178; Bacharach, C.A., 20, 1926, 2335; Caldwell, Jl. A.Ph.A., 7, 1928, 136; Krantz, Pract. Dr., 48, June, 1930, 57; Furman, Jl. Ind. Eng. Ch. (Anal Ed.), 2, 1930, 213; Kolthoff, *ibid.*, 2, 1930, 225; Sorensen, Jl. Soc. Ch. Ind., 50, 1931, 278T; Kenrick, C.A., 26, 1932, 2755; Johnson, Jl. A.Ph.A., 24, 1935, 397 and 498.

Gasometric Assays.—Anon., Chem. and Drug., 87, 1915, 41; Krantz, Jl. A.Ph.A., 21, 1932, 136.

Colorimetric Assays.—Arny and co-workers, Am. Dr., 60, 1912, 35; Proc. 8th Int. Cong. App. Ch., 26, 1912, 319; D-A. Ap. Zt., 33, 1913, 165; Dr. Circ., 57, 1914, 31; Jl. Frank. Inst., 180, 1915, 199; Jl. A.Ph.A., 4, 1915, 1294; Jl. Ind. Eng. Ch., 8, 1916, 309; *ibid.*, 11, 1919, 95; Jl. A.Ph.A., 12, 1923, 839; *ibid.*, 16, 1927, 116; A.J.P., 104, 1932, 272; Jl. A.Ph.A., 22, 1933, 195 and 956.

PART VI

THE DISPENSING OF PRESCRIPTIONS

CHAPTER LVIII

THE PRESCRIPTION

HAVING covered the entire field of special pharmaceutic operations and preparations, we can proceed to dispensing pharmacy and to that climax of the pharmaceutic art, the dispensing of prescriptions. Very properly, the prescription is the last topic studied in a course on pharmacy, for the preparation of prescriptions calls into play all the knowledge that belongs to an educated pharmacist. Not only must the prescriptionist know pharmaceutic manipulations and be well acquainted with all pharmaceutic preparations, but he must, moreover, be thoroughly familiar with all possibilities of chemical reaction, with the constituents of crude drugs, and, of course, must be well up on posology—dosage. However, we will leave the important topic of prescription criticism for subsequent pages, and this chapter will be devoted to the generalities of dispensing and to a discussion of the general character of the prescription —its composition, translating, and dispensing.

The *prescription* is an order written by the physician calling for medicines to be compounded and dispensed by the pharmacist.

Technically, the ideal prescription is supposedly divided into several parts, which can best be explained after presentation of a typical prescription.

Ideal Prescription

(Date.)			*August 6, 1936.*
(Name of Patient.)	FOR MRS. JONES		
(Superscription.) ℞.			
(Inscription.)	Acidi salicylici	ʒiij.	(Basis.)
	Potassii acetatis	ʒiv.	(Adjuvant.)
	Glycerini	℥j.	(Corrective.)
	Aquæ . . . . q. s. ad	℥iv.	(Vehicle.)
(Subscription.)	Misce fiat solutio.		
(Signa.)	SIG.—One teaspoonful four times a day.		
(Name of doctor.)			DR. BROWN.

Taking up the parts of the prescription in regular order, the following information may be of service.

The *date* of a prescription is rarely written by the physician, but is of value in establishing its identity.

The *name of the patient* should always be written by the physician, and especially the information as to whether the patient is an infant, child, or adult. If the doctor omits this important datum, the pharmacist should supply it by writing the name and address on the prescription or on the card to which it is attached. There is usually little difficulty in persuading the patient to furnish name and address. To this may be added the emphatic statement that whenever the name does appear, it should be written on the label. Suppose, in handling the medicine to two customers, an exchange is effected, and Mrs. Smith gets the remedy intended for Mrs. Jones. If the label bears the inscription "For Mrs. Jones," that inscription might prove a warning and secure the return of the medicine to the pharmacy. Of course, such an error on the part of the pharmacist is scarcely excusable, but such errors sometimes occur, and lucky is the man who is saved from the possible disastrous results of a slip of that kind by the simple precaution just given.

The *superscription* is the sign which is an abbreviation of the Latin word "recipio," meaning "take thou." The flourish at the end of the R is presumably the sign of Jupiter, legend saying that Roman physicians used the sign, thus making the superscription an invocation "take thou in the name of Jupiter." This pleasant fable has never, however, been well authenticated. The French use the abbreviation "P," meaning *prenez* or "take."

The *inscription* is the body of the prescription—the enumeration of the medicines desired and the quantity of each. As seen above, the inscription of the typical prescription may contain four groups of medicinal agents, although the modern physician is rapidly abandoning complex prescriptions, often prescribing a single ingredient.

Explaining these four groups:

The *basis* is the main ingredient—the medicine first indicated to the mind. Thus, in the above prescription (evidently for a rheumatic patient) the remedy first suggested was salicylic acid.

The *adjuvant* is the medicine intended to aid the basis in its medical action. In the above prescription the doctor evidently recalled that rheumatism is due to excess of uric acid, and decided to attempt to remove the uric acid by the use of the diuretic, potassium acetate. Hence this salt is the adjuvant—the assistant.

The *corrective* is some substance added to lessen irritating effect or improve flavor of the main ingredients. In the prescription given above glycerin is the corrective, but frequently flavored syrups or nonmedicated elixirs are used as corrective.

The *vehicle*, or *diluent*, is the material added to dilute the preparation to a reasonable dose. Too much stress cannot be laid upon the danger of prescribing small doses, such as a few drops of a liquid. In the hands of the ignorant or careless, fatal mistakes are apt to occur.

Most dangerous of all is the custom of some physicians in directing the patient to dilute a potent prescription at home. A fatal case of this kind occurring in Cleveland was the prescribing of tincture of aconite (U.S.P. 1890) for an infant, with the following remarkable directions: "Five drops in a glass of water, and then a teaspoonful every hour." The mother followed the directions implicitly, giving the babe five drops of the tincture in water, followed by a teaspoonful of the potent tincture.

The *subscription* includes the directions as to compounding intended for the guidance of the pharmacist. In the olden times the subscription was frequently quite lengthy, minute details of the compounding being written in choice Latin, but at present the subscription is usually boiled down to the succinct "M" or "M ft. pil." or "F.S.A." These terms are left untranslated, that the student may hunt up the abbreviations in the list of Latin terms found on a subsequent page.

The *signa* represents the directions to the patient, which directions are to be written on the label by the pharmacist, translating from Latin to English, if the physician gives the directions in the former language. Like the subscription, the signa was formerly written by the physician in Latin, but the modern medical man, not being as much at home with the classics as were his predecessors, rarely resorts to Latin, except a few time-worn abbreviations found in the list of Latin terms.

The modern physician, alas! pays but little attention to his prescription, and there is no part of the curriculum of medical colleges more neglected than the very important branch of prescription writing. It is sadly true that one reason why so many young physicians have gotten into the pernicious practice of prescribing ready-made nostrums is their apparent lack of training in correct prescription writing.

The following rules for prescription writing drawn up by an English physician are well worth repeating at this place—

Essentials for an Ethical Prescription

1. It should be carefully written on a sheet of note paper and not on a scrap of anything that comes handy.
2. It should preferably be written in ink.
3. It should contain the name (and probably also the address) of the patient for whom it is intended.
4. It should contain carefully worded directions for its use.
5. It should be initialed (or preferably signed) by its author.
6. When it contains dangerous ingredients, the words "not to be repeated" ought to be incorporated.
7. It should contain no incompatibility or any proprietary remedy, whose action is unknown to the author.

The pharmacist should do all in his power to dissuade the physician from reducing his "signa" to the stereotyped "as directed," since the dosage should appear on the label for the guidance of the patient, and on the prescription that the pharmacist may determine if the dose is safe. While on the question of dosage, mention should be made of the need of adoption, in this country, of the system regulating large doses that is in vogue in Germany. In that country an authoritative list of maximum doses is published, and any physician desiring to prescribe a dose larger than the maximum declares his intention by underscoring the dose, or rewriting the quantity in words.

As shown above, the ideal prescription is written in the Latin language, which is used because it is the universal language of science; because it lessens the use of local synonyms; and because it is frequently advisable to keep the patient from knowing the nature of the medicine prescribed.

Concerning the value of Latin as the universal language of science, suppose an actual case and imagine we have before us three prescriptions —one of an American practitioner, one written by a physician of Hanover, Germany, and the last the order of a doctor practising in Budapest, Hungary. Quite likely the pharmacist knows nothing of German, almost certainly he is not acquainted with the weird Hungarian tongue, yet were all three prescriptions brought to his store, he could read one as easily as the other, for all are written in Latin.

The other great value of the use of Latin is that it practically does away with the use of confusing synonyms. A person comes into a drugstore and asks for "chamomile," and the pharmacist has to inquire "which chamomile—German or Roman." Even so would it be if the doctor wrote his prescription in English and demanded "extract of chamomile." The question would again be, "which chamomile?" while if he writes "ext. anthemidis," or "ext. matricariæ," the chamomile he wants is very plain.

PRESCRIPTION LATIN

In the brief space of one chapter, much idea of Latin cannot be given, but the following explanations may throw at least some light on the Latin prescriptions.

In most English grammars we find that nouns are said to have three "cases"—nominative, possessive, and objective. Latin nouns have six such cases, but of these only two are used to any extent in pharmacy—the nominative and the genitive.

Those who have studied English grammar at all will remember that *the nominative case means that form of noun or pronoun used as the subject of the verb*; thus, "John" is nominative in the sentence "John runs"; likewise "I" in the sentence "I walk." In English the form of the noun is the same, regardless of its case. Not so, however, with pronouns, for while "I" is nominative, "me" is its objective form. Latin nouns have a different ending for each case, just as English pronouns differ according to case. Having thus described the nominative, we can turn to the genitive case, which has no exact counterpart in English. It comes nearest to our possessive case, but it really means what we would put in English as "of the ——," supplying the noun for the dash. A grouping of the terminations of the Latin noun in its various cases is called its declension, and the Latin nouns are grouped into five declensions, each having a different set of endings. Thus, in the first declension, we have—

Nominative, mensa (a table).

Genitive, mensæ (of a table).

and the plural of the same noun is

Nominative, mensæ (tables).

Genitive, mensarum (of tables).

In our limited space we cannot go beyond these few facts, and we will immediately proceed to practise the 2 cases as found in the Latin names of the Pharmacopœia:

First, let us look up a pharmacopœial name belonging to the declension just given—the first. This we find in two words, among many others, "tinctura" and "belladonna."

Nominative, tinctura (a tincture); "belladonna" (belladonna).

Genitive, tincturæ (of a tincture); belladonnæ (of "belladonna").

Let us bring these together in the official name, tincture *of* "belladonna" which in Latin is tinctura belladonnæ.

In the second declension we find two forms of nouns—masculine nouns ending in "us," and neuter nouns ending in "um." They are declined:

Nominative,	us	um
Genitive,	i	i

Let us apply these terminations, first picking out some official noun ending in "us"; for instance, "syrupus" and "rubus":

Nominative, syrupus (syrup); rubus (blackberry).

Genitive, syrupi (of syrup); rubi (of blackberry).

Combining these to read "syrup *of* blackberry," we get "syrupus rub*i*" (N.F. V).

Among the official nouns ending in "um," we find "unguentum" and "iodum."

Nominative, unguentum (ointment); iodum (iodine).

Genitive, unguenti (of ointment); iodi (of iodine).

Then the official name of "ointment *of* iodine" is "unguentum iod*i*." Of course, we can combine nouns of any declension, only being careful to employ the correct termination. Thus, we can write "tinctura iod*i*" (tincture *of* iodine) or "syrupus serpentari*æ*" (syrup *of* serpentaria).

The third declension embraces all those nouns whose genitive ends in "is." The nominative varies greatly, causing the declension to be complex, but all the official variations will be given here:

Nominative	*Genitive*
Adeps (lard).	Adipis (of lard).
Macis (mace).	Macis (of mace).
Sulfas (a sulfate).	Sulfatis (of a sulfate).
Sulfis (a sulfite).	Sulfitis (of a sulfite).
Mucilago (a mucilage).	Mucilaginis (of a mucilage).
Nux (a nut).	Nucis (of a nut).
Liquor (a solution).	Liquoris (of a solution).
Rhus (rhus).	Rhois (of rhus).
Flos (a flower).	Floris (of a flower).
Theobroma (theobroma).	Theobromatis (of theobroma).
Cantharis (cantharides).	Cantharidis (of cantharides).
Carbo (carbon).	Carbonis (of carbon).
Bos (ox).	Bovis (of the ox).
Pumex (pumice).	Pumicis (of pumice).
Cannabis (hemp).	Cannabis (of hemp).
Lotio (a lotion).	Lotionis (of a lotion).
Semen (a seed).	Seminis (of a seed).
Corpus (a body).	Corporis (of a body).
Cataplasma (a poultice).	Cataplasmatis (of a poultice).
Menthol (menthol).	Mentholis (of menthol).
Mel (honey).	Mellis (of honey).

In "rhus" we have a noun ending in "us" which does not belong to the second declension, and likewise the entire fourth declension ends in "us." Fortunately, there is but one pharmacopœial name involved in this declension; it being "spiritus" which is declined as follows:

Nominative, spiritus (a spirit). *Genitive,* spiritus (of a spirit).

To sum up, all pharmacopœial nouns ending in "um" take the termination "i" in the genitive; those in "a" in the nominative—except theobroma—take "æ" in the genitive; and all ending "us" in the nominative—except rhus, and spiritus—take "i" in the genitive; these rules applying only to the singular number.

Concerning the plural, we need only consider that of the first, second, and third declensions, exemplified in "herba," "folium," and "flos" respectively.

Singular		Plural	
Nominative	*Genitive*	*Nominative*	*Genitive*
Herba (an herb).	Herbæ (of an herb).	Herbæ (herbs).	Herbarum (of herbs).
Folium (a leaf).	Folii (of a leaf).	Folia (leaves).	Foliorum (of leaves).
Flos (a flower).	Floris (of a flower).	Flores (flowers).	Florum (of flowers).

So far we have considered the subject only in the simple relationship as seen in the names of the Pharmacopœia and of the National Formulary, and to make the matter still more clear, we will cite a few names where the application of the declensions may be seen:

Quinin*æ* sulf*as*,	Sulfate *of* quinine.
Sod*ii* sulf*is*,	Sulfite *of* sodium.
Mucila*go* acaci*æ*,	Mucilage *of* gum arabic.
Tinctur*a* nuc*is* vomic*æ*,	Tincture *of* nux vomica.
Liqu*or* calc*is*,	Solution *of* lime.
Fluidextract*um* rh*ois* glabr*æ*,	Fluidextract *of* rhus glabra.
Spirit*us* æther*is*,	Spirit *of* ether.
Tinctur*a* belladonn*æ* foli*orum*,	Tincture *of* belladonna leaves.
Tinctur*a* arnic*æ* flor*um*,	Tincture *of* arnica flowers.
Tinctur*æ* herb*arum* recent*ium*,	Tinctures *of* fresh herbs.

("Recentium" is an adjective, genitive plural, from the nominative singular "recens," and genitive singular "recentis.")

The official (or the Latin nominative singular) of "nux vomica," "rhus glabra," and "sodium" are the words just given.

We are now ready to consider the changes the Latin name undergoes in writing the prescription—a change that is quite marked, though very simple.

The sign ℞ means "take" and nothing else, and in the prescription we are not supposed to write—

"Take, sulfate of quinine," but, "Take, *of* sulfate of quinine," which means that in translating the prescription into Latin the word "sulfate" is put into the genitive, the same as is the word "quinine," and when correctly written, the term will stand—

"℞. Quinin*æ* sulfat*is*"
Take *of* sulfate *of* quinine (reversed, you see) and *not*—
"℞. Quinin*æ* sulfa*s*"
Take sulfate *of* quinine.

This is the only change in writing the pharmacopœial name in a prescription, although sometimes this change is perplexing; thus we write:

℞. Mucila*ginis* acaci*æ* and *not* ℞. Mucilag*o* acaci*æ*
(*of* mucilage *of* acacia) (mucilage *of* acacia).

Besides the nominative and genitive cases, the *ablative* case is used occasionally in pharmacopœial titles. Even as the genitive is used after the preposition "of," so the ablative is used after the prepositions "from," "with," "in," and "by." The following are the pharmacopœial instances of the ablative:

Hydrargyrum cum creta—mercury with chalk. In this case "creta" is the ablative singular of the noun of the first declension, creta.

Emulsum olei morrhuæ cum hypophosphitibus—emulsion of cod liver oil with hypophosphites. In this case "hypophosphitibus" is the ablative plural of the noun of the third declension, hypophosphis.

Ferri hydroxidum cum magnesii oxido—hydrated oxide of iron with oxide of magnesium. In this case "oxido" is the ablative singular of the noun of the second declension, oxidum.

The above outline refers only to Latin nouns. *Adjectives* change number and case with the noun they qualify, but their terminations do not necessarily conform with the termination of the noun. Thus, a masculine noun of the third declension may be qualified by a masculine adjective of the second declension. It simply changes to the same gender and case. Therefore it might be well to insert some adjectives found in pharmacopœial titles with their declensions:

FIRST AND SECOND DECLENSIONS

Singular

	Masculine	*Feminine*	*Neuter*
Nominative—	adhæsivus	adhæsiva	adhæsivum
Genitive—	adhæsivi	adhæsivæ	adhæsivi

Plural

	Masculine	*Feminine*	*Neuter*
Nominative—	adhæsivi	adhæsivæ	adhæsiva
Genitive—	adhæsivorum	adhæsivarum	adhæsivorum.

Adjectives of this class found in present and past pharmacopœial titles are:

Adhesivus	in emplastrum adhesivum	(adhesive plaster).
Amarus	in aurantium amarum	(bitter orange).
	in amygdala amara	(bitter almond).
	in vinum ferri amarum	(bitter wine of iron).
Ammoniatus	in tinctura guaiaci ammoniata	(ammoniated tincture of guaiac).
Benzoinatus	in adeps benzoinatus	(benzoinated lard).
Camphoratus	in tinctura opii camphorata	(camphorated tincture of opium).
Cantharidus	in collodium cantharidum	(cantharidal collodion).
Citratus	in caffeina citrata	(citrated caffeine).
Chlorinatus	in calx chlorinata	(chlorinated lime).
Compositus	in tinctura cinchonæ composita and a number of others	(compound tincture of cinchona).
Corrosivus	in hydrargyri chloridum corrosivum	(corrosive chloride of mercury).
Deodoratus	in tinctura opii deodorata	(deodorized tincture of opium).
Despumatus	in mel despumatum	(clarified honey).
Destillatus	in aqua destillata	(distilled water).
Dilutus	in acidum sulfuricum dilutum and a number of others	(diluted sulfuric acid).
Expressus	in oleum amygdalæ expressum	(expressed oil of almond).
Exsiccatus	in alumen exsiccatum	(exsiccated alum).
	in ferri sulfas exsiccatus	(exsiccated sulfate of iron).
	in sodii phosphas exsiccatus	(exsiccated phosphate of sodium).
Flavus	in hydrargyri oxidum flavum	(yellow oxide of mercury).
Fusus	in argenti nitras fusus	(fused nitrate of silver).
Granulatus	in ferri sulfas granulatus	(granulated sulfate of iron).
Induratus	in argenti nitras induratus	(hardened nitrate of silver).
Lotus	in sulfur lotum	(washed sulfur).
Mitigatus	in argenti nitras mitigatus	(mitigated nitrate of silver).
Monohydratus	in sodii carbonas monohydratus	(monohydrated carbonate of sodium).
Ponderosus	in magnesii oxidum ponderosum	(heavy oxide of magnesium).
Præcipitatus	in ferri sulfas præcipitatus and others	(precipitated sulfate of iron).
Reductus	in ferrum reductum	(reduced iron).
Saccharatus	in ferri carbonas saccharatus	(saccharated carbonate of iron).
Stypticus	in collodium stypticum	(styptic collodion).
Sublimatus	in sulfur sublimatum	(sublimed sulfur).
Sulfuratus	in calx sulfurata	(sulfurated lime).

The adjective *ruber* (example hydrargyri oxidum rubrum—red oxide of mercury) has same endings in the nominative and genitive cases as the other adjectives of the first and second declensions, except that the masculine nominative singular is ruber.

Third Declension of Adjectives

	Singular		*Plural*	
	Masculine and Feminine	*Neuter*	*Masculine and Feminine*	*Neuter*
Nominative—	Animalis	animale	animales	animalia
Genitive—	Animalis	animalis	animalium	animalium.

Adjectives of this class found in past and present pharmacopœial titles are:

Animalis	in carbo animalis	(animal charcoal).
Chirurgicalis	in liquor sodæ chlorinatæ chirurgicalis	(surgical solution of chlorinated soda).
Dulcis	in amygdala dulcis	(sweet almond).
Flexilis	in collodium flexile	(flexible collodion).
Glacialis	in acidum aceticum glaciale	(glacial acetic acid).
Levis	in magnesii oxidum levis	(light oxide of magnesium).
Mitis	in hydrargyri chloridum mite	(mild chloride of mercury).
Mollis	in sapo mollis	(soft soap).
Solubilis	in ferri phosphas solubilis and several others	(soluble phosphate of iron).

Some adjectives of the third declension have a slightly different form, viz.:

	Singular		*Plural*	
	Masculine and Feminine	*Neuter*	*Masculine and Feminine*	*Neuter*
Nominative—	adjuvans	adjuvans	adjuvantis	adjuvantia
Genitive—	adjuvantis	adjuvantis	adjuvantium	adjuvantium.

Three of these are used in U.S.P. or N.F. titles:

Adjuvans	in elixir adjuvans	(adjuvant elixir).
Effervescens	in pulvis effervescens compositus	(compound effervescent powder).
Recens	in tincturæ herbarum recentium	(tinctures of fresh herbs).

Three pharmacopœial titles have the adjectives in the comparative degree:

Aqua ammoniæ fortior	(stronger ammonia water).
Aqua aurantii florum fortior	(stronger orange flower water).
Aqua rosæ fortior	(stronger rose water).

Verbs are not used much in modern prescription writing beyond the stereotyped abbreviated phrases found in the list below. Moreover, a discussion of Latin verbs and their conjugation would mean a complete review of Latin grammar, which is clearly beyond the scope of this work. For further details, therefore, the reader is referred to list of books on pharmaceutic Latin found in Preface.

TABLE OF LATIN AND FOREIGN TERMS USED IN PRESCRIPTIONS
[(L.) Latin, (G.) German, (F.) French]

Term	Abbreviation	Meaning
Abendessen (G.),		Supper.
Ad (L.),		To, up to.
Adde (L.),	Add.	Let it be added.
Ad libitum (L.),	Ad lib.	At pleasure.
Alternis horis (L.),		Every other hour.
Ana (G.),	āā.	Of each.
Ante (L.),		Before.
Aqua bulliens (L.),	Aq. bull.	Boiling water.
Aqua fervens (L.),	Aq. ferv.	Warm water.
Aqua fontis (L.),	Aq. font.	Spring water.
Aqua pluvialis (L.),	Aq. pluv.	Rain water.
Alle drei Stunden (G.),		Every three hours.
Bene (L.),		Well, good.
Bis in die (L.),	B. i. d.	Twice a day.
Bissen (G.),		Bolus.
Bol (F.),		Bolus.
Capiat (L.),	Cap.	Let the patient take.
Capsulæ amylaceæ (L.),		Starch capsules (cachets).
Charta cerata (L.),	Chart. cer.	Waxed paper.
Chartula (L.),	Cht.	Papers.
Cochleare amplum (L.),	Coch. ampl.	Tablespoonful.
Cochleare magnum (L.),	Coch. mag.	
Cochleare medium (L.),	Coch. med.	Dessertspoonful.
Cochleare parvum (L.),	Coch. parv.	Teaspoonful.
Coletur (L.),		Let it be strained.
Collyrium (L.),	Collyr.	Eye wash.
Coquetur (L.),	Coq.	Let it be boiled.
Coucher (F.),		Bedtime.
Cuillerée à café (F.),		Teaspoonful.
Cuillerée à soupe (F.),		Tablespoonful.
Detur (L.),	Det.	Let it be given.
Dentur (L.),	Dent.	
Dentur talis dosis (L.),	Dent. tal. dos.	Give of such doses.
Deux (F.),		Two.
Dies (L.),	D.	Day.
Dividatur (L.),	Divid.	Let it be divided.

Term	Abbreviation	Meaning
Dosis (L.),		A dose.
Drachma (L.),	ʒ	A drachm.
Drei mal täglich (G.),		Three times a day.
Ejusdum (L.),		Of the same.
Enemata (L.),	Enem.	Enema.
Esslöffelvoll (G.),		Tablespoonful.
Et (L.),		And.
Ex modo prescripto (L.),	E. m. p.	As prescribed; as directed.
Fiat (L.),	Ft.	Let it be made.
Fois (F.),		Time.
Gouttes (F.),		Drops.
Granum (L.),	Gr.	Grain.
Guttæ (L.),	Gtt.	Drops.
Hora (L.),		An hour.
Hora somni (L.),	Hor. som.	At bedtime.
Jeder or jeden (G.),		Every.
Latwerge (G.),		Electuary.
Mica panis (L.),	Mic. pan.	Crumb of bread.
Misce (L).,	M.	Mix.
Mittagessen (G.),		Dinner (at noon).
Mitte talis dosis (L.),		Send of such doses.
Non repetatur (L.),	Non. rep.	Do not repeat.
Numero (L.),	No.	In number.
Oblate (G.),		Wafer paper.
Omni hora (L.),	Omn. hor.	Every hour.
Omni mane (L.),	Omn. man.	Every morning.
Omni nocte (L.),	Omn. noct.	Every night.
Optimus (L.),	Opt.	The best.
Pain azyme (F.),		Wafer paper.
Paquet (F.),		A powder (package).
Partes æqualis (L.),	P. æq.	Equal parts.
Pastillen (G.),		Lozenges.
Pillen (G.)		Pills.
Pilule (F.)		
Pondus civile (L.),		Avoirdupois weight.
Pondus medicinale (L.),		Apothecary weight.
Post cibum (L.),	Post. cib.	After eating.
Poudre (F.),		Powder.
Pro re nata (L.),	P. r. n.	As occasion requires (when needed).
Pulver (G.),		Powder.
Pulvis (L.),	Pulv.	A powder.
Pulvis subtillissimus (L.),	Pulv. subtil.	Very smooth powder.
Quantum sufficit (L.),	Q. s.	Sufficient quantity.
Quotidie (L.),		Daily.
Repetatur (L.),	Rept.	Let it be repeated.
Rotula (L.),		Globules.
Schlafengehen (G.),		Bedtime.
Scrupulum (L.),	℈	A scruple.
Secundum artem (L.),	S. a.	According to art.
Sesqui (L.),		Once and a half.
Signetur (L.),	Sig.	Let it be marked.
Solvetur (L.),	Solve.	Let it be dissolved.
Spiritus Vini Rectificata (L.),	S. V. R.	Alcohol.
Spiritus Vini Tenuis (L.),	S. V. T.	Diluted Alcohol.
Tabella (L.),	Tab.	A lozenge.
Talis (L.),		Of such.
Ter (L.),		Thrice.
Ter in die (L.),	T. i. d.	Thrice daily.
Tere bene (L.),		Rub well.
Theelöffelvoll (G.),		Teaspoonful.
Toutes les heures (F.),		All the hours (every hour).
Trois fois par jour (F.),		Three times a day.
Tropfen (G.),		Drops.
Uncia (L.),	℥	An ounce.
Ut dictum (L.),	Ut dict.	As directed.
Zwei (G.),		Two.

For a more complete list of Latin terms, see Scoville's "Art of Compounding."

While on the subject of abbreviations, mention should be made of the danger likely to arise from the careless writing of abbreviated names of drugs. Among classic instances of such abbreviations are "hyd. chlor.," which might mean chloral hydrate, mercuric chloride, or mercurous chloride; "liq. mag," which might mean solution of some magnesium salt, or else Magendie's solution (p. 926), while "sulf." may mean sulfate, sulfite, or sulfide; "nit." may mean nitrate or nitrite, and similarly an abbreviation of name of any negative element in salts and acids can be misconstrued when there is more than one acid derived from the element. In most cases of such abbreviation the experienced pharmacist can discern the remedy desired either by the dose prescribed or by the relative popularity of the several possibilities. Thus, a prescription calling for "zinc sulf." almost invariably means zinc sulfate, as the sulfite and sulfide of that metal are rarely used in medicine. This thought has been given fateful importance lately, when a number of deaths have resulted from the dispensing of barium sulf*ide* on prescriptions where barium sulf*ate* was intended (p. 530).

The *quantities* used in prescription writing are those of the apothecary, as shown in the typical prescription printed below. The metric system is used exclusively by the physicians of continental Europe, and to a slight extent by American physicians. Metric quantities are preferably expressed as shown in the prescription given below:

℞. Quininæ sulphatis	2.00
Ferri reducti	1.00
Acidi arsenosi	0.05

Misce fiat pilulæ numero xx.

In this country prescription blanks are sometimes printed with a vertical line intended to separate the grams from the fractional parts thereof, thus replacing the decimal points in the above prescription, just as in a ledger a line is used to separate dollars from cents.

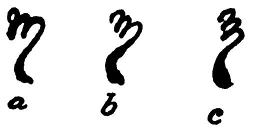


Fig. 278.—Faulty minim sign.

Rarely does the continental physician write the word "gramme"; quantities, as written above, being clearly understood as meaning the metric system.

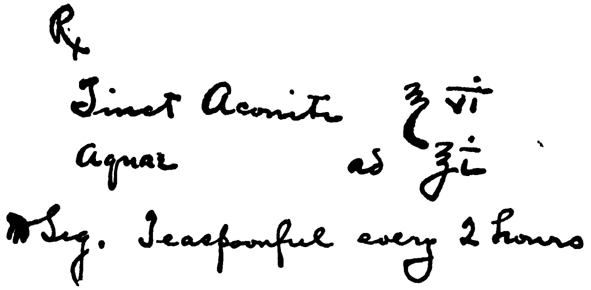
As abbreviations of drug names may sometimes lead to dangerous results through misinterpretation, so occasionally the abbreviations for quantities prove a source of error.

It is easy to write the symbol of ounce (℥) when drachm (ʒ) is intended, and there is still another danger lurking in the minim (♏) sign—a misunderstanding that resulted in the death of two persons in New Orleans some years since.

The minim sign seems distinct enough, but a prominent physician, now dead, gradually modified his minim sign (Fig. 278) from the correct form to one similar to the symbol for the drachm.

One day the physician wrote the prescription shown below, and the unfortunate

druggist, in one of those frightful lapses that might come to any of us, read and dispensed *six drachms* of tincture of aconite instead of the *six minims* desired.



℞

Tinct Aconite ʒvi

Aquae ad ℥ii

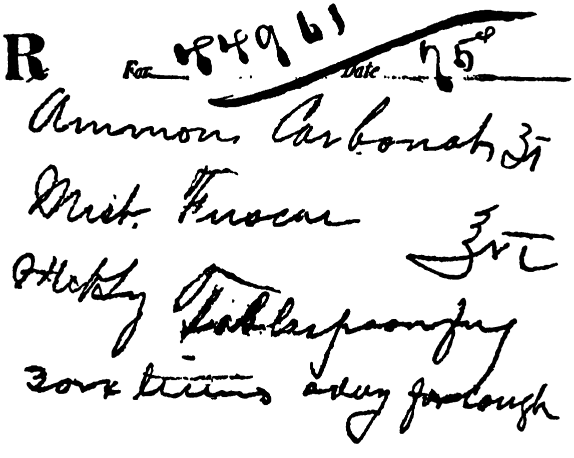
Sig. Teaspoonful every 2 hours

Fig. 279.—Dangerous prescription.

Of course, he was to blame, but when we hear of such things we should feel thankful that we were spared the fearful blunder. Naturally, the patient died, and the druggist, completely ruined, after a year of hopeless attempts of retrieving his fortune, gave up the conflict and committed suicide.

The metric quantities as written on page 1046 are less likely to mislead, although a fly speck might be mistaken for a decimal point. Another possibility of danger with physicians unfamiliar with the system is writing ten times the quantity intended. For instance, writing 0.05 (5 cg.) when 0.005 (5 mg.) was intended.

Before leaving the subject of the prescription as a document a few typical prescriptions may be of service.



R For 84961 Date 75

Ammon Carbonat ʒi

Mist Fuscae ℥vi

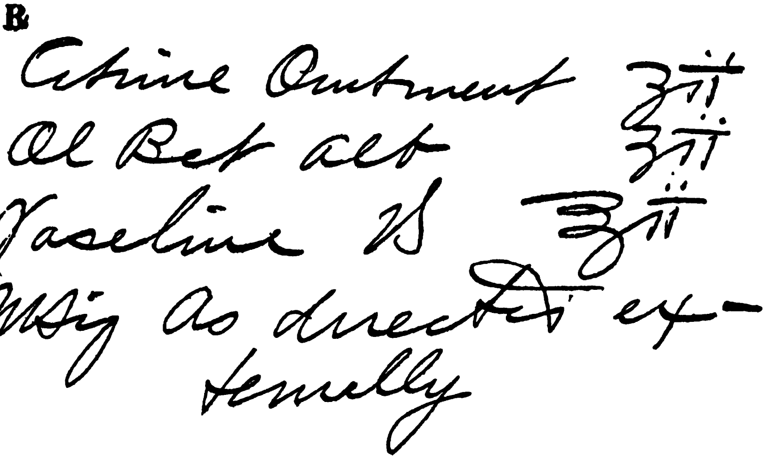
Sig. Tablespoonful 3 or 4 times a day for cough

Fig. 280.—Typical prescription.

Figure 280 is a clearly written prescription of a southern practitioner. As already explained, on page 279, *mistura fusca* is a local synonym for brown mixture.

Figure 281 is an equally clear prescription, written by a northern practitioner. What is "Ol. Bet. Alb."?

Figure 282, written by a Creole practitioner for a Creole patient, calls for Fowler's solution, a proprietary, "syrupus roborans," and the Solution



℞

Citrine Ointment ʒii
Ol Bet alt ʒii
Vaseline W ʒii
M Sig As directed externally

Fig. 281.—Typical prescription.

of Pepsin, U.S.P. 1880. The French directions are translated into English below:

2 cuillerées à café dans un verre d'eau après chaque repas.
2 teaspoonfuls in half glass of water after each meal.

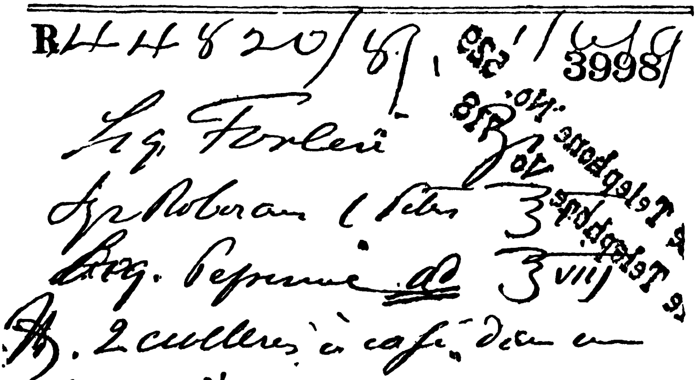
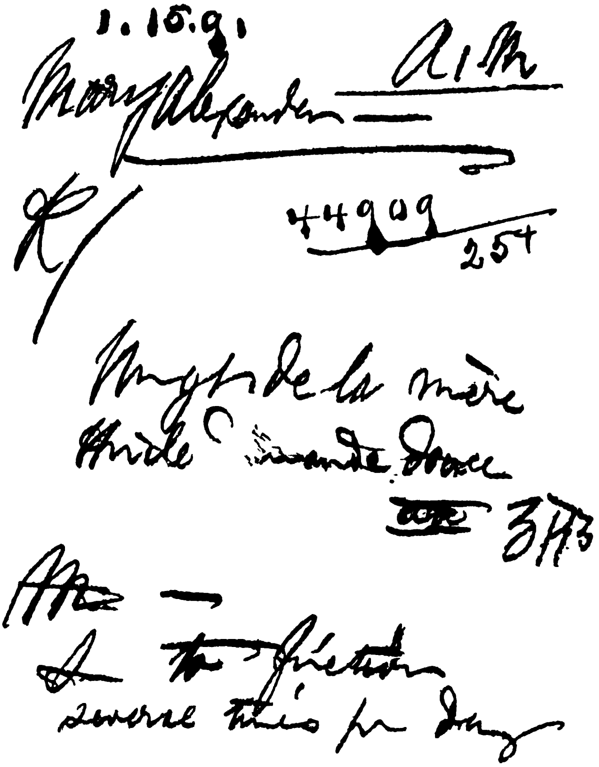


Fig. 282.—French prescription.

Figure 283 is written by a Creole physician for an American patient. The French ingredients are: Unguent de la mère (Unguentum Fuscum N.F. V.) and huile d'amande douce (oil of sweet almond).

Figure 284 is a clearly written prescription with French directions. Liquor Cinchonæ Cordifoliæ (B) is a special liquid extract of cinchona prepared by Battley and Co., of England. The English translation of directions is given below: Une petite cuillerée toutes les 3 heures. A teaspoonful every three hours.



1.15.91

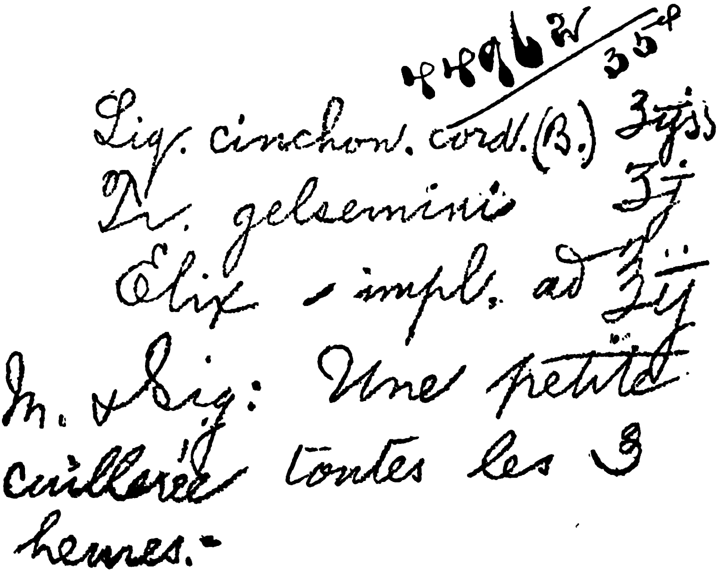
Mary Alexander A1M

R/ 44909 / 25¢

Onguent de la mère
Thècle ~~[illegible]~~ Once
~~[illegible]~~ ʒiij

~~Ap~~ —
~~S.~~ ~~th~~ friction
several times per day

Fig. 283.—French prescription.



44962 / 35¢

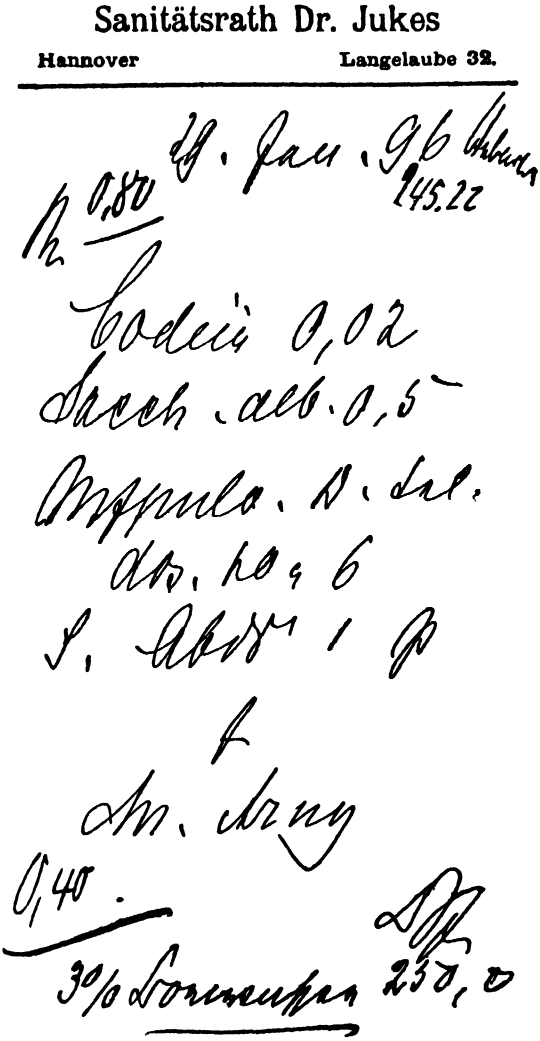
Liq. cinchon. cord. (B.) ℥ijss
Tr. gelsemini ℥j
Elix. simpl. ad ℥ij
M. & Sig: Une petite
cuillerée toutes les 3
heures.—

Fig. 284.—Typical prescription.

Figure 285 is written by a physician of Germany, calling for six powders (dent. tal. dos.), each containing 2 cg. of codeine and ½ Gm. of sugar. The directions read:

Abends ein Pulver.
Evenings a powder.

It being characteristic of the German prescription that the time of administration is written before the dose.



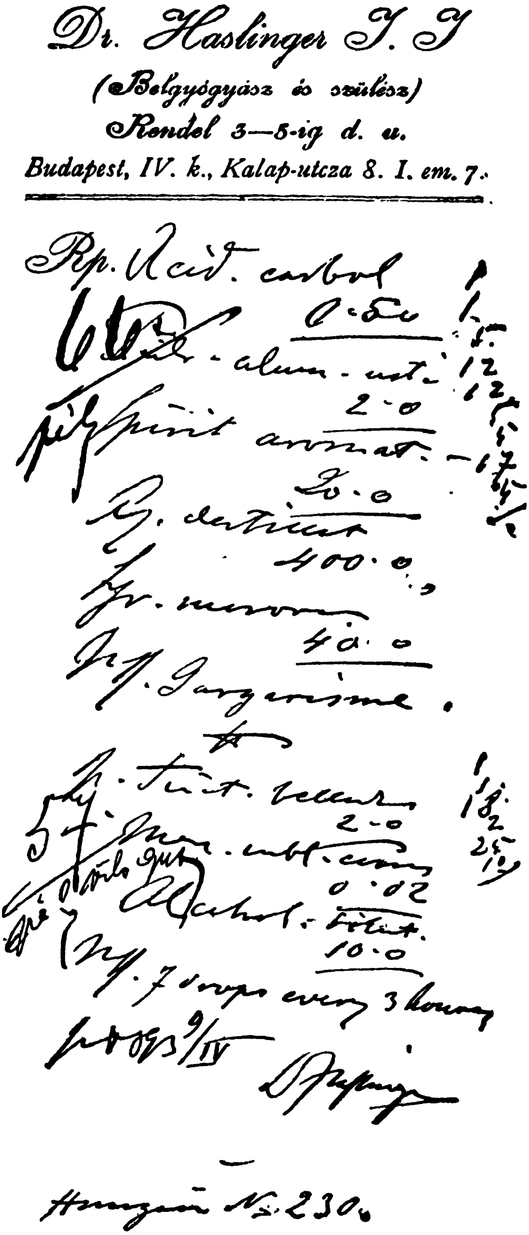
Sanitätsrath Dr. Jukes
Hannover Langelaube 32.

[illegible] Jan. 96
145.22
0,80
℞
Codeini 0,02
Sacch. alb. 0,5
[illegible] D. tal.
dos. No 6
S. [illegible] 1 P.
0,40
3% [illegible] 250,0

Fig. 285.—German prescription.

An interesting illustration of the convenience of the use of Latin in prescriptions is shown when the first and second prescriptions on Fig. 285 are compared. The first, written in Latin, could be compounded by any educated pharmacist in any part of the world. On the other hand, the second, written in German, is apt to prove a puzzler. It reads: 3 per cent Borwasser, 250 cc.

That is, a 3 per cent aqueous solution of boric acid is desired.



Dr. Haslinger J. J

(Belgyógyász és szülész)

Rendel 3—5-ig d. u.

Budapest, IV. k., Kalap-utcza 8. I. em. 7.

Rp. Acid. carbol 0·50

[illegible] alum. ust. 2·0

Spirit aromat. 30·0

Aq. destillat 400·0

[illegible] 40·0

M. D. S. Gargarisme.

Rp. Tinct. bellad. 2·0

[illegible] 0·02

Alcohol. [illegible] 10·0

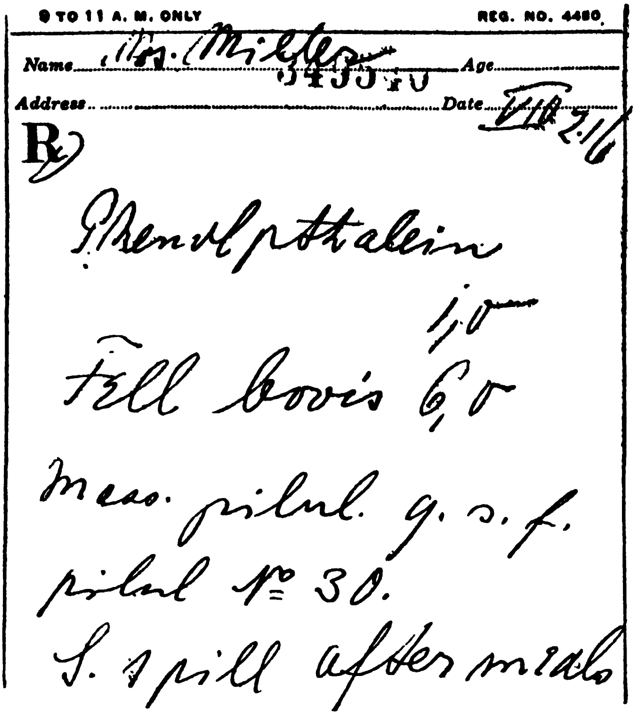
M. D. S. 7 drops every 3 hours

[illegible] 9/IV

Hungarian No. 230.

Fig. 286.—Hungarian prescription.

The prescriptions on Fig. 286 were written by a German physician residing in Budapest, Hungary, and both can be deciphered by a prac-



9 TO 11 A. M. ONLY REG. NO. 4450

Name Mrs. Miller Age

34335 x0

Address Date VIII 2.16

℞

Phenolphthalein 4,0

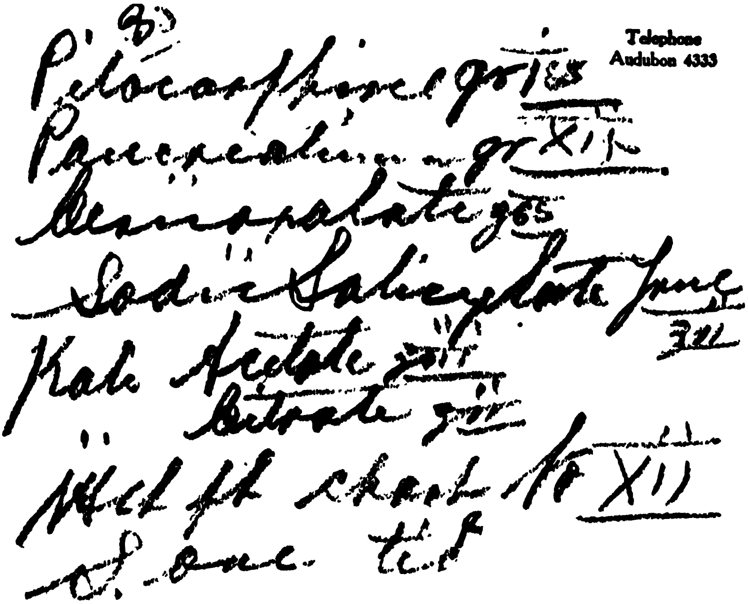
Fell bovis 6,0

Mass. pilul. q. s. f.

pilul No 30.

S. 1 pill after meals

Fig. 287.—Typical prescription.



Telephone
Audubon 4333

Pilocarpine gr 1/25

Pancreatin gr XII

[illegible] gr 5

Sodii Salicylate ʒ i

Kali Acetate ʒ ii

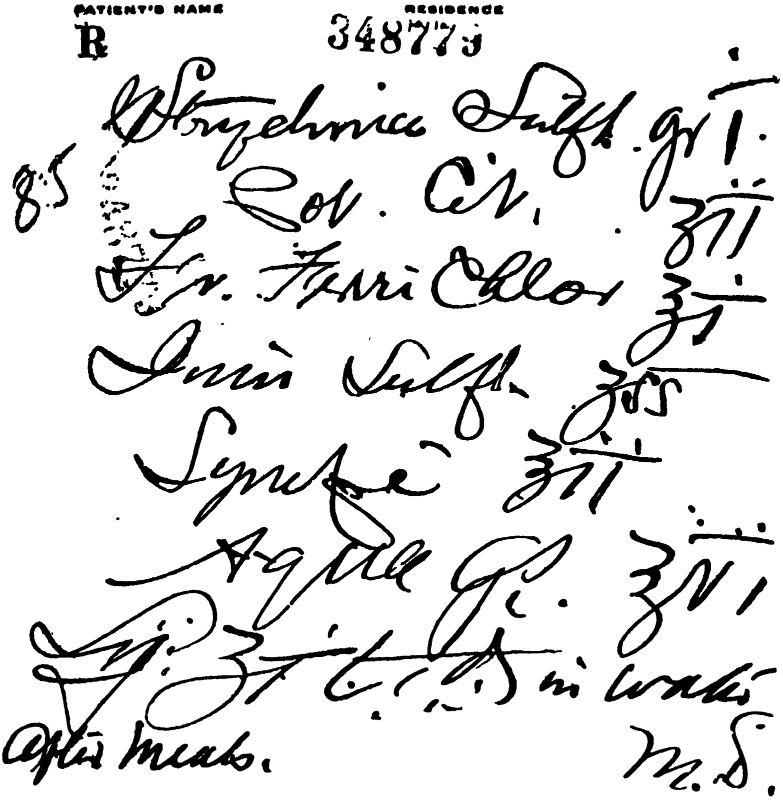
" Citrate ʒ ii

Misce fiat chart. No XII

S. one t.i.d.

Fig. 288.—Typical prescription.

ticed prescriptionist. For this reason they will not be translated by the writer. Mention, however, might be made of the figures on the right-hand side of the paper. In Germany, Austria, and Hungary, the price of every drug used in prescriptions, as well as the cost of containers and value of time spent in compounding, is carefully regulated by the government, and the figures above mentioned represent the summing up of values from the official schedule.



PATIENT'S NAME RESIDENCE

℞ 348773

Strychnia Sulph. gr i.

85 Pot. Cit. ℥ii

Tr. Ferri Chlor ʒi

Quin Sulph. ʒss

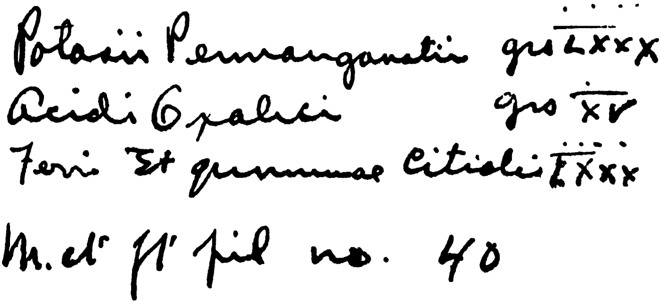
Syrupe ℥ii

Aqua q.s. ℥vi

M. ʒi t.i.d. in water

after meals. M.D.

Fig. 289.—Typical prescription.



Potassii Permanganatis grs LXXX

Acidi Oxalici grs XV

Ferri et Quininae Citratis LXXX

M. et ft. pil no. 40

Fig. 290.—Unusual Prescription.

Figures 287 to 290 are prescriptions recently written by physicians of New York City. Figure 290 is of such unusual character that it is discussed among incompatible prescriptions (p. 1070).

CHAPTER LIX

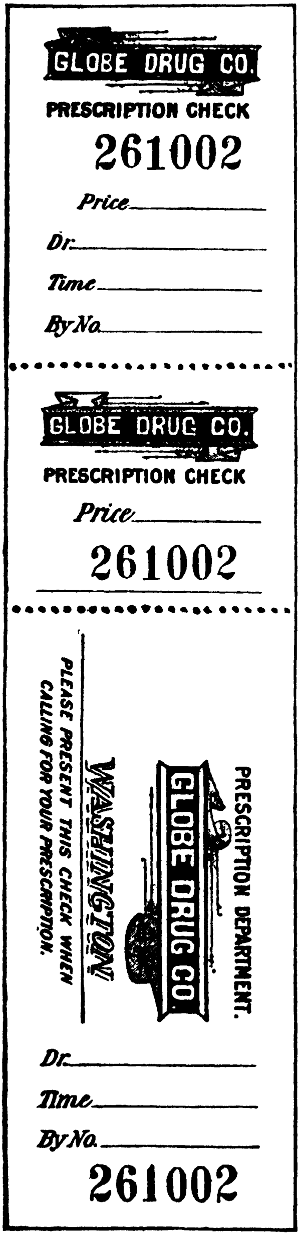
COMPOUNDING OF PRESCRIPTIONS

The prescription as a document is interesting, but of far greater importance is it that the pharmacist knows how to handle the prescription when it becomes his duty to compound it.

The work of the compounder of the prescription is manifold. He must know how to receive the prescription form and dispense the finished preparation to the customer; he must know how to label the container correctly; he must know how to fill the prescription; he must know how to scan it carefully for errors; and, lastly, he must know how to prepare or put up the medicine called for. To perform each step properly he must be intelligent, alert, tactful, skilful, careful, conscientious, and well informed.

Receiving the Prescription.—As mentioned above, if the prescription does not bear the name of the patient, the compounder should supply the deficiency, explaining it is a part of the system whereby mistakes are prevented. Cases are on record where fatal results have resulted from giving a properly prepared prescription to the person for whom it was not intended. This is most liable to occur if two persons are waiting for prescriptions written by the same doctor—say one for internal use; the other for a liniment. Hence the fact that the pharmacist hands the customer "Dr. Blank's prescription" is not a sufficient safeguard, since there may be two of Dr. Blank's prescriptions being compounded at the same time.

In large stores the giving of checks to the person leaving the prescription is a safeguard against such mistakes. A form for such checks is shown below, the one section being given to the customer, one attached to the prescription, and the third attached to the package (Fig. 291). A simpler method is giving the customer a numbered brass check and writing


GLOBE DRUG CO.
PRESCRIPTION CHECK
261002
Price__________
Dr.__________
Time__________
By No.__________

GLOBE DRUG CO.
PRESCRIPTION CHECK
Price__________
261002

PRESCRIPTION DEPARTMENT.
GLOBE DRUG CO.
WASHINGTON
PLEASE PRESENT THIS CHECK WHEN CALLING FOR YOUR PRESCRIPTION.
Dr.__________
Time__________
By No.__________
261002

Fig. 291.—Prescription check.

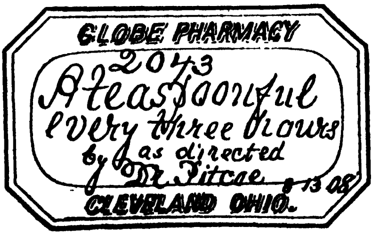

GLOBE PHARMACY
2043
A teaspoonful
every three hours
as directed
by Dr. Pitcae 8 13 08
CLEVELAND OHIO.

Fig. 292.—Typical label.

same number on prescription and package. Safest of all, however, is the securing of name and address of patient.

Dispensing the finished preparation to the customer is brought up chiefly to introduce the subject of the relation of the compounder and dispenser; to emphasize the need of that rare gift, *tact*. This gift cannot be acquired by reading books, and the writer feels he can do no more than suggest the importance of tact on the part of the dispenser by citing a few typical cases.

A woman comes into a store asking for 5 grains of calomel and 5 grains of *salt*. The pharmacist, realizing that a prescription had been written and not presented, lest more should be charged for the goods if furnished on a prescription than when sold on verbal order, emphasizes the possible formation of mercuric chloride in such a mixture, tactfully interrogates until the woman admits that a prescription was written, and convinces her that this prescription must have called for calomel and *soda*, and persuades her to bring the prescription.

A man comes in with a printed prescription calling for pills containing several well-known tonics, and also "jerubebin, 1 grain." Instead of telling the man that the prescription is a fraud (a statement for which the mind of the dupe is prepared by the skilfully worded circular sent by the "philanthropist" who furnishes prescriptions "free"), the pharmacist quietly brings out Druggists' Circular (1884, p. 138), in which the fraud is exposed. The testimony afforded by this disinterested source convinces even the credulous chap who is saved the dollar he was to send the donor of the prescription "in case the medicine cannot be obtained elsewhere."

A man who once had a prescription wrongly compounded insisted on sitting behind the prescription counter watching the compounder, so as to keep tab. To make things still safer, he usually plied the compounder with questions. The new clerk was a young man just from college; the man, more suspicious than ever, was more persistent in questioning. "What's this medicine?" he inquired, pointing to the then little-known abbreviation "antipy." "Oh," said the youth, nonchalantly, "that's Latin for the new medicine, phenyl-dimethyl-pyrazolon." From that day forth the man considered the youth the smartest and most reliable druggist in town.

A nervous woman wants to know what a certain prescription she holds in her hand is good for, and what are its constituents. The tactful pharmacist responds that these are questions which the physician who wrote the prescription is alone permitted to answer, and expresses his willingness to place the lady in telephonic connection with the doctor. His kindly offer is declined.

Fig. 293.—Prescription numbering machine.

The only other phase of dispensing to be considered is the question of containers and wrapping of the same. This subject is given consideration on pages 310 to 313, so here it is only necessary to say that the pharmacist who values his prescription business, picks out the best glassware, finest corks, and most refined boxes and printing.

Labeling the containers is worthy of a special paragraph, as often the effect of the choicest labels is marred by blurred or scratchy, uncouth, or overflourished writing. A severely plain, heavily shaded back hand, written with the blackest ink and allowed to dry without blotting, makes the most attractive form of label, but of late typewriting has largely replaced handwriting on prescription labels. A strikingly written prescription label is shown in Fig. 292. It will be noted that the body of this label contains neither lines nor printing; that the filled-in part of label is a symmetric whole; that the printing is severely plain and as concise as possible. All the data on the label are essential; the number, the name of the physician, the directions, and the date should appear on each label.

In some States the law directs that the name of the compounder should be put on the container, in which event a small gummed slip, "Dispensed by—," attached to the bottom of the package or bottle usually suffices. It is an excellent practice to have labels intended for external use printed on glazed red paper, this affording a striking contrast to the white paper label for internal preparations. Then, of course, the pharmacist should be provided with slips bearing such frequently used directions "shake well"; "for external use," etc.

Filing Prescriptions.—As the prescription is more or less of a legal document, it is important that the pharmacist carefully preserves either the original or a duplicate. In this country the original is kept by the pharmacist, although the question as to who owns the prescription—the patient or the pharmacist—has been and still is a matter of legal controversy. It would be interesting if the several conflicting court opinions on this matter could be settled for once and all by a decision from the United States Supreme Court. In Germany it is the universal custom to return the prescription to the patient, the pharmacist keeping a carefully checked copy.

The first step toward preserving the prescription for future reference is giving it a number. These numbers run consecutively and are written on the prescription with date and price. One pharmacist known to the writer started new numbering each year, marking the first prescription compounded on January 1st as No. 1, stringing all the prescriptions of one year on a long piece of ⅛-inch brass wire, the files of each year being hung on a row of nails driven in the walls, each nail labeled for the year. This plan is *not* to be commended, for whenever it chanced that the date on the label was faded, it necessitated looking up the same number on possibly a dozen files.

Many establishments now use consecutive numbering machines, such as the one shown in the appended cut (Fig. 293). Such machines consist of a stamping apparatus, which automatically changes the type of the numbers one unit higher each time an impression is made, thus precluding the possibility of giving two prescriptions the same number. In the more expensive varieties the same number can be repeated in duplicate (or even triplicate), thus enabling the compounder to number the prescription and label before the machine progresses one unit higher. However, the suggestion that the entire label be written renders a duplicate numbering machine unnecessary.

Several ways of preserving prescriptions are in vogue in this country.

Filing on String or Wire.—This method, outlined just above, and variations of it, is not very satisfactory. The hole in the prescription, when pierced by the wire (or by the needle, if string is used), may cut out a part of the wording most needed. The weight of the pile of prescriptions bearing down and rubbing against a lead-penciled prescription is apt to blur it beyond recognition, while the long file hung on the wall catches dust and soon becomes filthy.

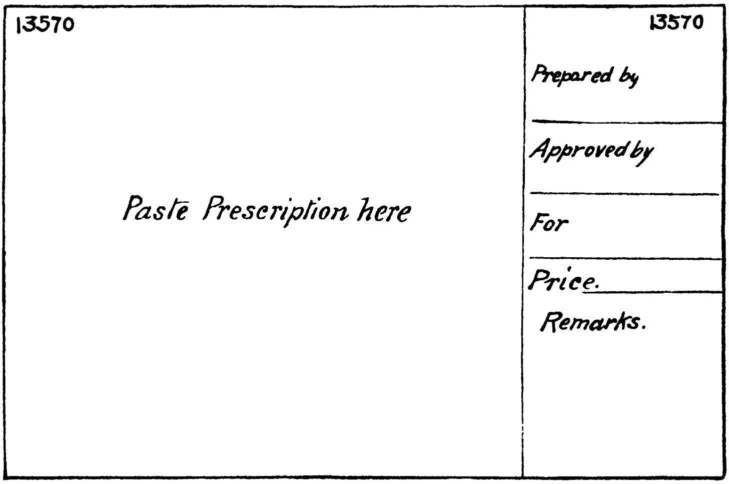
Pasting in a Scrapbook.—This method is quite satisfactory, although the handling and storing of big scrapbooks are sometimes inconvenient.

Writing a Copy in a Blank Book and Filing or Returning Originals.—This method, used by all pharmacists of Germany and by a few prescriptionists of America, entails a large amount of work and is apt to lead to errors unless the copy is carefully checked against the original by a second person, as in proofreading.

Wrapping the Prescriptions in Packages of 100 and Packing Ten Con-

secutive Hundreds in a Wooden Box.—This method was used by Dr. A. E. Ebert, and there are on the market one or more patented files embodying the same idea. The prescriptions are thus kept perfectly clean, but on opening a package to get the desired prescription, there is danger of the others being mislaid or blown away if the prescriptions are not bound together in some manner. The patented prescription filing devices provide against this contingency.

Pasting to a Card Which is Filed in a Cabinet.—This method, a result of the modern filing card cabinet craze, is by all means the most satisfactory method of filing the prescription. The best form of card is that shown below (Fig. 294), with marginal space on which all data can be written, thus leaving the prescription intact.



13570

Paste Prescription here

13570

Prepared by

Approved by

For

Price.

Remarks.

Fig. 294.—Prescription filing card (reduced).

In event of success of the present movement looking toward the abolition of the repetition of prescriptions by the pharmacist unless so directed by the physician, the question of filing prescriptions will become less important, since in such case the prescription will be referred to less frequently.

In these days pharmacists have to exercise the utmost care in filing prescriptions for narcotics, special regulations being in effect under the national narcotic law. These prescriptions must either be kept on a separate file or a record book must be kept giving the number, date and other particulars. Except those calling for "exempt" narcotics, these prescriptions may not be refilled. Prescriptions for narcotics must bear the physician's registry number and name and address of patient and date. It is incumbent upon the pharmacist to satisfy himself that the prescription is presented in good faith and not for the purpose of evading the narcotic law.

Scanning for Errors.—This heading opens the important topic of the tact required by the pharmacist in dealing with the physician.

The pharmacist must always carefully study the prescription to note possible errors as to dosage and dangers as to incompatibility.

If such errors are found, the customer should be dismissed with some excuse and with the promise to "send it around," and the physician approached as to his real intention. This duty is the most delicate that falls to the pharmacist. If he telephones the doctor with the blunt message "Haven't you made a mistake?" he is apt to gain a life enemy. If, on the other hand, he calls on the physician, remarking something about being uncertain as to the physician's intention, casually mentioning that his construction of the prescription means a pretty stiff dose, asking if drachms were meant instead of his reading of ounces, the physician is usually glad to take this loophole of escape and will accept the question made by the druggist, inwardly deciding that the druggist possesses tact as well as knowledge. If diplomacy fails, as it sometimes does with a fool who masquerades as a professional man, rough-shod tactics should be employed, and the druggist should then—*and only then*—tell the doctor that the dose is excessive, backing his statement by printed authorities, such as the dispensatories, and declining to fill the prescription unless the doctor repeats the quantity, *written in words.*

In all cases where the doctor is in error he is quite anxious that the patient does not learn of the blunder, and in the controversy in question the pharmacist should let the doctor know that the prescription will be returned to the patient with the reason why it was not dispensed. Of course, in this case the adage "be sure you're right, then go ahead" must be religiously observed by the druggist.

Necessarily, the druggist must do everything in his power to maintain the most cordial relations with the physician, but this does not mean that he must supinely submit to injustice. A few examples of this phase of the prescriptionist's experience may be of service.

The "blind prescription," the prescription that can be put up only by a few favored druggists, is a nuisance that can and should be immediately stamped out by reporting the offenders—the doctor, to the local medical association; the pharmacist, to the local druggists' association.

Two examples of such blind prescriptions are found on p. 917, in the two names for quinine sulfate. The synonym "sulfatis Americanis Australis" was written in good faith by the physician, who desired to keep the patient from knowing she was taking quinine, and who cheerfully furnished the information to the druggist, while the doctor who perpetrated "sulphat de pelletiere" told the patient the prescription could be prepared only by a druggist blocks away, and furnished the information to the neighboring druggist only after a sharp talk.

A certain "Dr. Jones" wrote a prescription, "Dr. Jones' rheumatic mixture," telling the patient that it could be obtained at a certain remotely situated drug store. The druggist to whom it was presented called on the doctor and politely asked to be favored with the recipe. It was forthwith furnished with abundant explanations.

Compounding the Prescriptions.—The preparing of each prescription is a law to itself, the blending of the ingredients called for depending entirely on the individual peculiarities of the medicines so blended. In the foregoing pages of this book information has been given of most substances used in American medicine, as well as the methods of compounding various classes of preparations. If this information has been absorbed, the compounding of prescriptions becomes simple—merely the application of principles already learned. At this place, therefore, we need only discuss the technical phases of compounding as it peculiarly applies to the prescriptions, and also the question of incompatibility.

Special Technic of Prescription Compounding.—As just mentioned, the routine compounding of a prescription calling for pills is similar to the directions given for the manufacture of pills on page 330, for emulsions, as explained on page 281, and for all other preparations, as outlined in the proper place on the foregoing pages. This done, the compounder should always verify his results by the so-called *"checking system"*; that is, after the prescription is compounded, the finished preparation and the written prescription are handed to the second person, while the compounder repeats the prescription, laying special emphasis on the quantity of each ingredient. This checking system should be used in every pharmacy, no matter how small. If there is but one skilled compounder in the store, he should train the boy to check with him, and if the compounder is by himself, he should check his own work by placing each bottle containing the medicine used in a row on the counter, with the weight employed immediately in front of the bottle. This precaution might be criticized as meaning an outlay for extra weights, but this expenditure is more than compensated for by the security coming from the plan.

In Case of Error.—Perhaps this title seems superfluous, since, of course, no errors should occur, but the writer agrees with an experienced pharmacist who said that whenever he heard of a druggist's mistake he simply thanked God that he was not the offender. Mistakes are liable to occur to all, hence the compounder should guard continually against errors, for even one of these may blast the pharmaceutic reputation of a lifetime.

The handling of an error calls for the highest possible tact, hence no fixed and fast rules can be given, except the general statement that an attempt to explain by lying usually makes matters worse. Of course, whenever possible, the error should be repaired without exciting the suspicion of the customer, such as intercepting the messenger or requesting return of medicine, but at all hazards the damage must be repaired even if it is necessary to call the prescribing physician to your aid. This last step, disastrous as it is to the pharmacist, should be taken only in extreme cases.

INCOMPATIBILITIES

The word "incompatibility" means "lack of agreement," and when the several ingredients in a prescription do not agree, such mixture is said to be incompatible. Prescription incompatibility is grouped into three classes, according to the nature of the disagreement: *pharmaceutic* (or physical) incompatibility; *chemical* incompatibility, and *therapeutic* incompatibility. These we will consider in regular order.

Pharmaceutic incompatibility is that form of disagreement depending chiefly on the question of relative solubility. Thus a solution of resinous substance, say, tincture of ginger, will become turbid on addition of water, not because of any chemical change, but because the resin, while soluble in alcohol, is not soluble in alcohol diluted with water. Likewise, a gum in aqueous solution—like mucilage of acacia—will be precipitated on addition of a strongly alcoholic tincture, simply because the gum is insoluble in diluted alcohol. A third typical case of pharmaceutic incompatibility that might be cited is the classic prescription calling for quinine, sulfuric acid, and a licorice preparation (p. 917). The reason for giving this case special emphasis is because, at first glance, it seems a case of chemical incompatibility, since it deals with the active principle of licorice, glycyrrhizin. But since it is based entirely upon the solubility of glycyrrhizin in acid, and not with the chemical decomposition of the glycyrrhizin, it is an example of pharmaceutic incompatibility.

Among pharmaceutic incompatibilities, for the want of a better place, we group such prescription experiences as the dispensing of deliquescent salts, the compounding of pill prescriptions calling for excess of liquid, and those cases where not enough solvent is directed.

Chemical incompatibility is that form of disagreement where a chemical change occurs when two or more substances are blended. Sometimes the chemical change improves the product, and such cases are not considered as incompatibilities. An example of this is the well-known prescription calling for mercuric chloride and potassium iodide (p. 618), when a soluble potassio-mercuric iodide is formed. Such cases are rare, however, being limited to the formation of hydroxides from oxides, the neutralization of a base by an acid, and a few special reactions such as the saponification of an oil by addition of alkali.

In the modern conception of solution it is considered that chemical action usually conforms with the following rule:

A chemical reaction occurs between two soluble bodies only when one or more products of such a reaction is either insoluble or gaseous. Always apply the above rule. Thus, if NaCl and KBr be mixed, will there be a reaction? What would be the products of such a reaction? Naught but KCl and NaBr—both soluble bodies—hence no reaction occurs. On the other hand, if we added a solution of NaCl to a solution of $AgNO_3$, a reaction would occur because one of the possible reaction products—AgCl—is insoluble.

Hence the whole question hinges on the solubility of the reaction products, and the table of solubilities, given on page 141, will be of great value in considering this question.

Among the more important cases of precipitation (hence of incompatibility) are the following:

1. *The formation of an insoluble salt* (as in the case just cited).

If Part V, dealing with chemical analysis, has been carefully studied, the most likely forms of such precipitation will have been learned, thus:

(*a*) The alkali metallic ions, lithium, sodium, potassium, and ammonium, are hardly likely to be precipitated by any chemical (p. 458). Exception: Potassium salts plus tartaric acid may precipitate potassium bitartrate.

(*b*) The alkaline earth ions—barium, strontium, calcium, and magnesium—will be precipitated on addition of carbonates and phosphates.

(*c*) The third, fourth, fifth and sixth groups of metallic ions will be precipitated by the carbonates, phosphates, hydroxides, and sulfides.

This statement must be taken in a general way. Thus, with several of the metals, the precipitated hydroxide is redissolved by excess of alkaline hydroxide, and, in truth, arsenic is not precipitated by an alkaline hydroxide.

(*d*) The seventh group of metallic ions—silver, lead, and mercuric salts—will be precipitated by all the foregoing, and also by chlorides and sulfates.

Besides these general rules, the special precipitants explained as tests in Part V will, of course, act as incompatibilities.

2. *Formation of special insoluble organic salts,* such as tannate of iron (ink), when tannin-bearing drugs are combined with iron salts; meconate of lead, when opium preparations are combined with lead solutions; and the production of the insoluble blood-red iron salicylate when iron preparations are combined with salicylates.

3. *Precipitation of alkaloids by alkaloidal reagents* (p. 901). Example of this is the precipitation of the cinchona alkaloids when preparations of this drug are combined with potassium iodide and mercuric chloride.

4. *Formation of insoluble bodies when synthetic organic chemicals are combined with certain reagents.* An example of this is the formation of green crystals when antipyrine is treated with spirit of nitrous ether that has become acid.

5. *Formation of insoluble bodies when certain organic chemicals are decomposed by certain reagents,* such as the decomposition of chloral, by action of alkali, into chloroform (p. 666).

To give extended examples of these incompatibilities, beyond the outline given above and the mention made of these individual peculiarities in discussion of the chemicals in Parts III and IV, would take too much space, hence for complete enumeration of incompatibilities the reader is referred to Ruddiman's admirable work on "Incompatibilities," mentioned in Preface.

Incompatibilities due to liberation of gases may be summed up as *explosive prescriptions,* combinations where carbon dioxide is evolved with that mild form of explosion called *effervescence;* and those few cases where gaseous ammonia may be liberated from ammonium salts.

Explosive prescriptions must be known in advance by the compounder, as otherwise an explosion may occur, producing dangerous results. As already explained (p. 471), explosions are produced by a sudden evolution of gases, and all substances liable to produce such gaseous evolution on trituration must be handled with the utmost caution. Already in Parts III and IV we have learned most possibilities of this kind, so here a sketchy summary will suffice:

(*a*) All oxidizing agents, such as potassium chlorate, chromic acid, potassium permanganate, silver oxide, hydrogen dioxide, and nitric acid, are liable to explode when combined with organic matter, and such oxidizable inorganic matter as sulfur or charcoal.

(*b*) Hypophosphites are liable to explode when heated above 100° C., or when combined with any substance (such as *nitrates* and other oxidizing agents) liable to produce phosphine (PH_3).

(*c*) A modification of "*a*" is the fact that strong nitric acid and its preparations effervesce with drug preparations containing tannin and with oil of turpentine, sometimes with explosive violence.

(*d*) Iodine is liable to explode when treated with ammonia or with oil of turpentine.

Effervescent Prescriptions.—When any acid combines with a carbonate, carbon dioxide is evolved with an effervescence which is harmless if allowed to proceed in an open dish. If the ingredients are mixed in a bottle which is immediately corked, the force of the compressed gas is enough to blow out the cork or possibly shatter the bottle. Hence, as already mentioned on page 504, such mixture should be prepared in graduate or mortar, and the liquid poured into the bottle with only a slight "bead." Aside from a clearly discernible combination of carbonate and acid, look out for prescriptions calling for carbonates and those pharmaceuticals containing acetic acid, such as syrup of squill.

Likewise bismuth compounds frequently effervesce when combined with carbonates and bicarbonates (p. 332).

Combinations Liberating Ammonia.—Such prescriptions are rare, being practically confined to combinations of ammonium chloride and lime or of solution of ammonium salts with solution of soda and solution of potassa.

Therapeutic incompatibility is that form of disagreement where the doctor prescribes two medicines that are therapeutically antagonistic. Examples of this are the blending of a stimulant with a sedative, of a mydriatic, like belladonna, with a miotic, like physostigma; of pepsin with alkali, and of pancreatin with acids. The combining of pepsin and pancreatin is also condemned by the best medical authorities.

An interesting case of therapeutic incompatibility recently reported was the painting of a wound with tincture of iodine and then applying a moist mercuric chloride dressing. Mercuric iodide was produced with serious results.

The question of therapeutic incompatibility is entirely beyond the province of the pharmacist, the writer's experience being that the doctor, no matter how friendly, resents suggestions from the druggist along this line.

Handling Incompatible Prescriptions.—The question of the compounding and dispensing of incompatible prescriptions can best be considered in discussion of each of the several examples of incompatible prescriptions given on the pages which follow.

Discussing the subject in a general way, it can be said that the question—both as to compounding and dispensing—is a matter of good judgment.

Every pharmacist should know an explosive prescription at sight, should know those which should not be combined under any circumstances (such as chromic acid and glycerin), and those which can be mixed if proper precautions are taken (such as mixing nitric acid and oil of turpentine). Explosive prescriptions are usually a menace to the compounder rather than to the customer, hence self-interest behooves complete knowledge of this class of prescriptions.

In other forms of incompatibility the pharmacist is confronted with two important questions: 1. "Is the prescription safe to dispense?" 2. "How can it be least objectionably compounded?"

As to dispensing, there are frequently cases of *intentional incompatibility*—cases where the doctor really desires an unsightly mixture, because of its therapeutic virtue. We all know that the official chalk mixture is of value because of the insoluble chalk it contains; even so the prescription calling for zinc sulfate and lead acetate must be dispensed containing the precipitate of lead sulfate, since that constitutes a large part of the healing effect of the mixture.

On the other hand, prescriptions in which potent medicines are produced in insoluble form, such as those prescriptions in which powerful alkaloids are precipitated, should be viewed with suspicion by the compounder, and while it is often an exceedingly delicate matter to approach the physician on the subject, it is usually best to let the doctor know, either at the time or later, the possibility of danger. No pharmacist of tact or good sense will bluntly announce to the customer that he will not compound such a prescription, but will always consult the physician. In all cases where this kind of prescription is dispensed, a "shake well" label must be put on the bottle.

Of course, there are prescriptions of this kind which must not be dispensed, such as the mixture of chloral hydrate and an alkali cited above, and in the list of prescriptions which follows mention is made of those which are unsafe to dispense.

A last word on consulting the physician about dangerous incompatibility as well as dangerous doses. Always approach him armed with accepted authority. On dosage, the Pharmacopœia and the National Formulary can be cited, while on incompatibilities, Ruddiman's book is the best guide.

The question as to the best way of compounding an incompatible prescription depends on the individual prescription, and in the line of incompatible prescriptions which follows, the best way of compounding is usually given. In a general way it might be stated that when the two substances likely to react are diluted as much as possible before mixing, the chances of incompatibility are lessened, as was discussed on page 420.

Another important question of compounding is, "When is the pharmacist justified in changing a prescription?" The answer is that a change is justified only when such change improves the prescription without affecting its medicinal action. A few examples may be cited:

(*a*) A prescription calling for a certain alcoholic tincture mixed with gummy substances may precipitate the gum. If the equivalent amount of the fluidextract is used, the precipitation may be avoided.

(*b*) An aromatic water, when used to dissolve a salt like potassium iodide, has some of its oil separate, and cloudy mixture results. If the salt is dissolved in the smallest quantity of water and then mixed with the aromatic water, no oil will separate.

(*c*) A prescription called for phenol mixed with an amount of water insufficient to dissolve it. If a part of the water—say one eighth or one quarter—be replaced by glycerin, a perfect solution ensues.

(*d*) Pills calling for ferrous sulfate, U.S.P., or other crystalline salts are found to yield a mass that is too soft. By use of the proportional quantity of exsiccated salt the mass can be easily made. Most of these or similar cases are given among the prescriptions cited on the pages which follow, so this short summary suffices at this place.

In conclusion let it be said that when a change is made, it is always best to let the physician know, explaining why the change was made.

INCOMPATIBLE DANGEROUS OR UNUSUAL PRESCRIPTIONS

Below are printed 138 prescriptions that are sufficiently out of the ordinary to justify careful attention by the student. In order to afford students practice, the criticisms are not given along with each prescription, but are found on pages 1073 to 1083. These prescriptions have been copied as written and the wording is not necessarily pharmacopœial.

1.	℞.	Tinct. iodi	ʒij
		Liniment ammoniæ	℥iv.
	M.	Ft. lint.	
2.	℞.	Spiritus ætheris nitrosi	℥ss
		Fluidext. uvæ ursi	℥iss.
3.	℞.	Acidi chromici	gr. x
		Glycerini	℥ss.
4.	℞.	Olei terebinthinæ	℥iv
		Acidi nitrici	ʒiv.
5.	℞.	Argenti oxidi	gr. v.
	M.	Ft. pilulæ No. xx.	
6.	℞.	Zinci oxidi	ʒij
		Zinci carb. præc	ʒj
		Petrolati	ʒss
		Liq. calcis	ad ℥iv.
7.	℞.	Quin. sulfatis	gr. x
		Potass. acetatis	gr. xx
		Acidi sulfurici	gtt. x
		Aquæ	q. s. ad ℥ij.
8.	℞.	Tinct. guaiaci	15
		Mel depurati	15
		Kali chlorati	13
		Syr. acaciæ	q. s. 90.

9.	℞.	Ammonii carbonatis	gr. xxiv
		Ferri et ammon. cit	ʒj
		Glycerini	℥ss
		Aquæ	ad ℥viij.
10.	℞.	Camphor	2
		Tincture of benzoin	12
		Acetic acid	40
		Rose water to make	120.
11.	℞.	Potassium citrate	ʒij
		Spirit of nitrous ether	℥ss
		Syrup of orange	℥ss
		Water, to make	℥ij.
12.	℞.	Potass. chlorat	ʒj
		Boracis	ʒss
		Hydrarg. perchlor	gr. xx
		Glycerin	ʒij
		Aquam	ad ℥iv.
13.	℞.	Potass. cyanidi	gr. j
		Acidi citrici	gr. v
		Syrupi pruni virg	℥iv.
	M.	Dessertspoonful.	
14.	℞.	Ammon. chloridi	90 grains
		Vini ipecac	160 minims
		Syrupi	1½ ounces
		Ext. glycyrrh. liq	80 minims
		Aq. anisi	ad 4 ounces.
15.	℞.	Potass. brom	ʒij
		Chloralis	ʒj
		Spts. ammon. arom	℥ss
		Syrupi aurant. cort	℥ij
		Aquæ	ad ℥iv.
16.	℞.	Rectified oil of tar	ʒj
		Oil eucalyptus	ʒss
		Oil thyme	ʒss
		Creosote	ʒss
		Oil sage	♏xx
		Simple syrup	q. s. Oj.
17.	℞.	Bismuth et ammon. cit	gr. xxx
		Liquor pepsini	℥j
		Elix. et aquæ	āā ad ℥iv.
18.	℞.	Copaibæ	℥iv
		Olei cubebæ	gtt. xx
		Calcis	gr. xx.
19.	℞.	Solution of potassium citrate	℥iv
		Citrated caffeine	
		Urotropin	
		Potassium acetate	āā ʒij
		Peppermint water	℥ij.
20.	℞.	Acid. hydrocyan. dil	♏xx
		Tincturæ iodi	♏xv
		Aquæ	ad ℥j.
21.	℞.	Argenti nitratis	gr. v
		Micæ panis	gr. xx.
	M.	Ft. pilulæ No. xx.	
22.	℞.	Codeinæ phosphatis	gr. viij
		Sodii citratis	ʒij
		Syr. acidi hydriod	q. s. ℥iv.

23.	℞.	Tinct. cannabis ind.	8
		Sodium bromide	15
		Tinct. valerian	8
		Water, to make	120.
24.	℞	Syrupi ferri iodidi	℥iss
		Potassii iodidi	ʒj
		Potassii carbonatis	ʒiss
		Syrupi tolutani	℥ss
		Aquæ	℥ij.
25.	℞.	Quininæ bisulfatis	ʒss
		Misturæ Bashami	℥ij.
26.	℞.	Potassii bromidi	ʒiv
		Aquæ menth. piperitæ	℥vj.
27.	℞.	Potassii bicarbonatis	ʒj
		Tinctura guaiaci ammon	ʒij
		Mucilaginis acaciæ	ʒij
		Quininæ sulfatis	gr. viij
		Acidi sulphuric. arom.	ʒiv
		Aquæ	ad ℥iv.
28.	℞.	Tincturæ guaiaci ammoni	℥ij
		Spiritus ætheris nitrosi	℥ss
		Aquæ cinnamomi	ad ℥iv.
29.	℞.	Potassii bromidi	gr. xv
		Liq. bismuthi et ammon cit	ʒj
		Sodii bicarbonatis	gr. xv
		Ol. menthæ piperitæ	♏j
		Aquæ chloroformi	ad ℥ss.
30.	℞.	Cocain. alk	gr. xvj
		Chloroform	ʒj
		Phenol	♏v
		Ol. amygd. am	℥j.
	M.	Ft. sol.	
31.	℞.	Acidi phosphorici	ʒij
		Acidi nitrici	ʒv
		Tincturæ ferri chloridi	ad ℥ij.
32.	℞.	Ext. ergot. liq	ʒiij
		Ext. hydrast. liq	ʒiij
		Tinct. nucis vom.	ʒij.
33.	℞.	Hydrargyri chloridi corros	gr. ¾
		Strychninæ sulfatis	gr. j
		Quininæ sulfatis	ʒj
		Liquor acidi arsenosi	ʒj
		Tincturæ ferri chloridi.	ʒij
		Misturæ ferri et ammon. acet.	ad ℥iv.
34.	℞.	Tincturæ myrrhæ	ʒij
		Morphinæ acetatis	gr. j
		Acidi tannici	ʒss
		Syrupi zingiberis	℥j.
	M.	Ft. sol.	
35.	℞.	Hydrargyri bichloridi	gr. j
		Liq. potass. arsenitis	gtt. xlviij
		Syrupi ferri iodidi	ʒvj
		Elixir cinchonæ	ad ℥vij.

36. ℞.	Cocainæ hydrochlor	gr. ij
	Sodii boratis	gr. x
	Aquæ	℥j.

M. Ft. sol.

Sig.—Apply to eye.

37. ℞.	Hydrarg. bichlorid	gr. j
	Potassii iodidi	ʒiij
	Tincturæ cinchon. comp	℥viij.

M. Ft. sol.

Sig.—Teaspoonful thrice daily.

38. ℞.	Hydrarg. subchlor	ʒss
	Ungt. aq. rosæ . . . ad	℥j.

39. ℞.	Tinct. guaiac	℥ss
	Sol. potass. hydr	℥ss
	Alcohol	℥ss
	Cinnamon water to make	℥ij.

40. ℞.	Argenti nitratis	gr. 1/6
	Bismuthi subnitratis	gr. ij
	Ext. belladonnæ fol	gr. 1/12.

Dent. tales dos. No. x.

41. ℞.	Quininæ bisulfatis	ʒj
	Sodii hyposulfitis	ʒiiss
	Glycerini	℥j
	Aquæ cinnamomi . . . ad	℥iv.

M.

Sig.—Shake and take a teaspoonful one hour before meals, in water.

42. ℞.	Potass. iodid	ʒij
	Sodii carb	ʒj
	Tr. nux vom	ʒiv
	Liq. arsenicalis	ʒij
	Aq . . . ad	℥viij.

43. ℞.	Potassii citratis	ʒiij
	Potassii bicarbonatis	ʒiij
	Tincturæ belladonnæ	ʒiiss
	Aquæ menth. piperitæ . . . q. s. ad	℥viij.

44. ℞.	Exsiccated ferrous sulfate	1 grain
	Ext. aloe	1 grain
	Apiol	1 minim
	Oil savin	1 minim.

M. Ft. d. t. d. 24 pills.

45. ℞.	Ethanol	
	Solution of hydrogen peroxide (10 vols.) . . . āā	℥ss.

M. Sig.—Ear drops.

46. ℞.	Sodium phosphate	2½ ounces
	Sodium bromide	½ ounce.

Directions.—Teaspoonful four times a day in water.

47. ℞.	Tragacanth	225 grains
	Mercury oxycyanide	15 grains
	Glycerin	1½ ounces
	Oil lavender	15 drops
	Distilled water, to make	12 ounces.

48. ℞.	Salicylic acid	2 drachms
	Solution of ammonium acetate	2 fluidounces
	Spirit of nitrous ether	½ fluidounce
	Syrup	½ fluidounce.

Directions.—Two teaspoonfuls every three hours until relieved.

49.	℞.	Sodium arsenate	1
		Oxyquinalone	1
		Potass. dichrom	9
		Distilled water	q. s. 300.
	M.	Sig.—For trench mouth.	

50.	℞.	Infus. digitalis	
		Liq. ferri et amm. acet	āā ℥iv.

51.	℞.	Phenylhydrazine hydrochloride	2.00.

Make into 20 capsules.

52.	℞.	Iron pyrophosphate	2 drachms
		Diluted phosphoric acid	3 fluidrachms
		Syrup	q. s. ad 3 fluidounces.

Directions.—Teaspoonful in water an hour after meals.

53.	℞.	Betanaphthol	8 grains
		Precip. sulfur	1 drachm
		Alcohol	4 drachms
		Saturated solution of zinc sulfate	
		Saturated solution of sulfurated potassa	
		Of each, enough to make	4 ounces.

54.	℞.	Tannic acid	4
		Alum	4
		Dobell's solution to make	120.

55.	℞.	Calc. hypophosphitis	ʒiv
		Liquor potassii arsenitis	ʒj
		Tinctura ferri chloridi	ʒj
		Strychninæ sulfatis	gr. j
		Acidi phosphorici dil	ʒj
		Aquæ	ad ℥iv.

56.	℞.	Ferri et quininæ citratis	ʒiv
		Tincturæ valerianæ ammoniatæ	ʒvj
		Aquæ	q. s. ℥xij.

57.	℞.	Sodium salicylate	ʒiij
		Sodium bicarb	
		Sodium citrate	
		Sodium bromide, of each	ʒvi.
		Distilled water, to make	℥viij.

58.	℞.	Tincturæ opii	℥ss
		Liq. plumb. subacet. dil	q. s. ad Oj.

59.	℞.	Argyrol	8
		Albolene, to make	60.

60.	℞.	Quininæ sulfatis	gr. xxx
		Tincturæ ferri chloridi	ʒj
		Syrupi et aquæ	āā ℥j.

61.	℞.	Quininæ hydrochloratis	3.0
		Antipyrine	2.0
		Aquæ destillatæ	5.0.

62.	℞.	Hydrarg. chlor. mitis	gr. xx
		Antipyrine	gr. xl.
	M.	Ft. pulv. No. xx.	

63.	℞.	Strontium bromide	2 drachms.
		Fowler's solution	30 drops
		Tincture of belladonna	2 fluidrachms
		Elixir of glycerophosphates	1 fluidounce
		Elixir of gentian, to make	4 fluidounces.

64.	℞.	Potassium iodide	2 drachms
		Tincture of ferric chloride	3 fluidrachms
		Infusion of quassia, enough to make.	6 fluidounces.

65.	℞.	Ammon. carb	gr. ij
		Amidopyrin	gr. iij
		Tr. opii camph	♏xij
		Spt. æth. nit	♏vij
		Tr. aconiti	♏ss
		Syr. cocillana. comp	♏x
		Liq. potass. cit	q. s. ʒj.
	D. t. d. No. xxii.		

66.	℞.	Radicis gent. pulv	gr. xi
		Radicis rhei pulv	gr. xvi
		Radicis zingib. pulv	gr. viii
		Sodii bicarbonatis	gr. lxxx
		Aq. menth. pip	ad ℥vii.
	M.	Ft. mist.	

67.	℞.	Zinc chloride	4 grains
		Dobell's solution	3 ounces.
	M.	Sig.—Mouth wash.	

68.	℞.	Acetylsalicylic acid	1 drachm
		Amidopyrine	1 scruple
		Sodium bicarbonate	30 grains.
	Mix and make 30 capsules.		

69.	℞.	Cocain. hydrochlor	gr. v
		Menthol	
		Chloreton	āā gr. x
		Liq. petrolat	℥j.
	M.	Ft. sol.	

70.	℞.	Balsam of Peru	4 drachms
		Sulfur	1 ounce
		Salicylic acid	6 drachms
		White petrolatum	6 ounces.
		Make an ointment.	

71.	℞.	Natri. bicarb	ʒij
		Kali. bicarb	ʒiv
		Magnes. sulf	ʒxij
		Aquæ	ʒvi.

72.	℞.	Syr. scillæ	ʒiv
		Syr. ipecac	ʒij
		Spt. æth. nit	ʒiij
		Syr. pruni virg	℥ij.

73.	℞.	Ext. belladonnæ	gr. j
		Pulv. camphor	℈j
		Acetanilidi	℈j
		Salolis	℈j
		Strych. sulf	gr. 1/10.
	M.	Fiant caps. No. x.	

74.	℞.	Potass. chlorat.	
		Sodii. hyposulfit	āā ʒj
		Ol. gaultheriæ	gtt. xii.
	M.	Fiant pulv. No. xii.	

75.	℞.	Phenolphthalein	gr. xv
		Betanaphthol	ʒiss
		Salol	ʒij
		Menthol	gr. xx.
		Mix and divide in 30 Konseals.	

76. ℞.	Plumbi acet	gr. xxx
	Acid. acet. dil	ʒij
	Syr. tolutan	ʒiv
	Syr. limonis	℥iss
	Aq. cinnamon. ad	℥vi.

Misce.

77. ℞.	Atropinæ. sulf	gr. j
	Strychnin. hydrochlor	gr. ij
	Acid. salicylic	gr. iij
	Sodii biborat	gr. ij
	Aquæ destillat. ad	℥iss.

Misce.

78. ℞.	Tr. ferri chlor	ʒij
	Potass. chlorat	ʒj
	Glycerin	ʒiij
	Liq. potass. cit q. s.	℥iij.

79. ℞.	Ammonium carbonate	2 drachms
	Potassium iodide	1 drachm
	Spirit of ether	2 fluidrachms
	Chloroform water, enough to make	6 fluidounces.

80. ℞.	Tincture of ferric chloride	4 fluidrachms
	Hexamethylenamine	2 drachms
	Water enough to make	6 fluidounces.

Make a solution.

81. ℞.	Potassium iodide	2 drachms
	Diluted hydrobromic acid	4 fluidrachms
	Chloroform water enough to make	6 fluidounces.

Make a solution.

82. ℞.	Potassium iodide	3 drachms
	Potassium bromide	2 drachms
	Sodium sulfate	1 ounce
	Spirit of nitrous ether	4 fluidrachms
	Infusion of buchu, enough to make	6 fluidounces.

83. ℞.	Acid gallic	ʒj
	Ext. ergot. liq	ʒiss
	Acid. tannic	ʒij
	Tinct. ferri perch	ʒi
	Mag. sulf	ʒiij
	Aq ad	℥xij.

Sig.—℥j. o 4h.

84. ℞.	Potass. bromid	ʒiij
	Sod. salicyl	ʒiij
	Caff. citrat	grs. xl
	Aq. dest ad	℥vj.

℥ss. o 4h.

85. ℞.	Phosphori	gr. 1/25
	Pulv. cinchonæ	gr. j
	Pulv. nucis vom	gr. ss
	Ferri redact	gr. ij.

Ft. pil. Mitte xxiv.

86. ℞.	Sod. salicyl	ʒv
	Potass. brom	ʒiij
	Acid. hydrobrom. dil	ʒiij
	Aq ad	℥viij.

87. ℞.	Potass. iodid	gr. xx
	Iodi	gr. x
	Ext. bellad. vir	ʒi
	Adipis praep ad	℥ij.

88.	℞.	Camphor	
		Menthol, of each	10 grains
		Phenol	6 grains
		Iodine (cryst)	4 grains
		Ephedrine (alk)	1 per cent.
		Liq. petrolatum, to make 2 ounces.	

89.	℞.	Aluminis	ʒij
		Glycerini boracis	℥j
		Glycerini acidi tannic	ʒvi
		Aquam	ad ℥viij.

90.	℞.	Iodi (resubl.)	gr. vij
		Sodii chlorid	gr. xxv
		Aq. dest	q. s. Oj.

91.	℞.	Cacao butter	12.0
		Oil sweet almonds	15.0
		Sulfur precipitated	3.0
		Resorcin	1.5
		Oil rose	0.4.

92.	℞.	Balsam of Peru	
		Ointment of zinc oxide, of each	15.0.
		Mix.	

93.	℞.	Acid. nitrohydr. dil	ʒss
		Tr. cardam. comp	℥iss.

94.	℞.	Protargol	2.0
		Cocaine hydrochlorate	0.5
		Distilled water	60.0.
	Sig.—External use.		

95.	℞.	Camphor	1 grain
		Salol	1 grain
		Aspirin	2 grains
		Citrated caffeine	1 grain.
		Of such doses, 12 capsules.	

96.	℞.	Epinephrine (1–1000)	ʒj
		Antipyrin	
		Resorcinol, of each	gr. vi
		Normal saline solution to make	℥j.

97.	℞.	Oleoresinæ aspidii	4.0
		Olei terebinthinæ	2.0
		Olei ricini	60.0.
	Sig.—Use at one dose.		

98.	℞.	Fol. digital	gr. j
		Sodii nitritis	gr. ss
		Strych. sulf.	gr. 1/24
		Ferri sulf. exsicc	gr. ij.
		D.t.d. pil. No. xx.	

99.	℞.	Potassii permanganatis	gr. lxxx
		Acidi oxalici	gr. xv
		Ferri et quininæ citratis	gr. lxxx.
	M.	Ft. pilulæ No. xl.	

100.	℞.	Sodii brom	ʒj
		Acetanilid	gr. viii
		Sodii phosph	℥i
		Spt. ammon. arom	ʒiv
		Aquæ	q. s. ℥iv.

101.	℞.	Codein. sulf	gr. iij
		Acid. hydrocyan. dil	gtt. xx
		Spt. chloroformi	ʒiv
		Syr. simpl	℥ss
		Aq. dest. q. s.	℥iij.

102.	℞.	Morphine sulfate	4 grains
		Methenamine	2 drachms
		Calomel	20 grains
		Sodium citrate	1 ounce
		Potassium iodide	3 drachms
		Elixir of terpin hydrate to make	4 ounces.

103.	℞.	Hydrast. acet	gr. ij
		Acid. boric	gr. x
		Sodii borat	gr. xx
		Tr. opii deodor	♏xv
		Aq. dest. q. s.	℥j.

104.	℞.	Potass. bicarb	ʒv
		Liq. strych	ʒiss
		Inf. gent. comp ad	℥vi.

105.	℞.	Resorcin	0.50
		Ol. menth. pip	0.25
		Magnes. ust	16.00
		Calcii carb	8.00.
	M.	Ft. pulv. No. xxiv.	

106.	℞.	Strych. sulf	gr. j
		Potass. brom	ʒvij
		Aq q. s.	℥viij.
		Ft. mist.	

107.	℞.	Zinc sulfate	1 grain
		Boric acid	6 grains
		Sodium borate	4 grains
		Camphor water, to make	1 ounce.

108.	℞.	Quininæ sulfatis	gr. j
		Acid. sulfatis dil	♏j
		Potass. iod	gr. v
		Aq	ʒj.

109.	℞.	Ferri valerianatis	
		Quin. valerianatis	
		Ammon. valerianatis āā	gr. j.
		Misce pil. No. j.	
		D.t.d. No. xii.	

110.	℞.	Potass. iodidi	gr. xx
		Quininæ disulfatis	gr. vij
		Syr. calc. lactophosph. ad	℥ij.
	M.	Ft. mist.	

111.	℞.	Sodii chloridi	ʒij
		Acid. boric	ʒij
		Quin. hydrochlor	ʒss
		Thymol	gr. x
		Aq. camph ad	℥xx.

112.	℞.	Asafœtida	gr. ss
		Ol. carui	♏ij
		Ext. anthemid	gr. iss
		Ext. gentianæ	gr. ij
		Ext. nucis vom	gr. 1/8.
	Ft. pil. Mitte xxiv.		

113. ℞.	Acetylsalicylic acid		1.2
	Methenamine		1.2
	Water, to make		60.0.

114. ℞.	Sulfur		2 drachms
	Menthol		1 drachm
	Resorcin		1 drachm
	Rose water to make		16 ounces.

115. ℞.	Acidi carbolici		gr. x
	Camphoræ		ʒiij
	Aquæ		ʒij
	Glycerini	ad	℥j.

116. ℞.	Phenol		20 drops
	Sodium bicarbonate		4 drachms
	Magnesium carbonate		3 drachms
	Glycerin		4 drachms
	Peppermint water, to make		8 ounces.

117. ℞.	Potassium iodide		64 grains
	Sodium nitrite		32 grains
	Syrup of orange		1 drachm
	Chloroform water to make		8 ounces.

118. ℞.	Ammon. chlor		3
	Theobrom. sod. salicyl		8
	Aq. menth. pip	q. s.	180.

119. ℞.	Acid hydrochlor. dil		ʒiv
	Tr. nucis vom		ʒiss
	Ext. glycyrrh. liq		ʒiv
	Inf. gent. comp	ad	℥vi.

120. ℞.	Iodoform		2.0
	Balsam of Peru		8.0
	Petrolatum, to make		120.0.

121. ℞.	Tannic acid		30 grains
	Extract of belladonna		1 grain
	Ichthyol		30 grains.
	Oil of theobroma enough to make six rectal suppositories.		

122. ℞.	Calcium lactate		15.0
	Dionine		0.1
	Syr. simpl		15.0
	Aq. dest	q. s.	180.0.

123. ℞.	Acidi citrici		ʒj
	Petrolati		ʒij
	Adipis lanæ		ʒj
	Petrolati liquidi		ʒij
	Ceræ albæ		ʒj
	Aquæ		℥j
	Olei limonis		gtt ij.
	Misce et fiat unguentum.		

124. ℞.	Ammon. mur		ʒj
	Syr. ipecac		ʒj
	Spt. æth. nitrosi		ʒvj
	Syr. tolu	q. s.	℥vi.

125. ℞.	Creosote carbonate		2 drachms
	Mucilage of acacia		enough
	Peppermint water		1 ounce
	Syrup of tolu, to make		4 ounces.

126. ℞.	Bismuthi subnitrat		12
	Tr. opii camph		24
	Tr. catechu		8
	Elix. simpl	q. s. ad	90.

127.	℞.	Deodorized tincture of opium		2 drachms
		Tincture of belladonna		2 drachms
		Magma of bismuth, to make		8 ounces.
128.	℞.	Zinc sulfate		8 grains
		Alum (powd.)		6 grains
		Colorless hydrastis (Lloyd)		2 drachms
		Distilled water, to make		3 ounces.
129.	℞.	Ungt. iodi		ʒiss
		Ungt. hydrarg. fort		ʒss.
130.	℞.	Calc. chlor		gr. xxx
		Sodii sulfat		℥j
		Syr. zingib		℥j
		Aq. cinnamon	ad	℥viii.
131.	℞.	Sod. cit		ʒiv
		Calc. brom		ʒiij
		Syr. pruni virg		℥j
		Aq. dest	q. s.	℥iij.
132.	℞.	Magnes. sulfat		ʒvj
		Sodii phosph		ʒvj
		Aquam	ad	℥vj.
133.	℞.	Sodium bromide		7 drachms
		Sodium citrate		7 drachms
		Peppermint water, to make		3 ounces.
134.	℞.	Acetanilide		24 grains
		Sodium bromide		1½ grain
		Potassium bromide		1 drachm
		Syrup of orange, to make		3 ounces.
135.	℞.	Sodium hyposulfite		4 drachms
		Menthol		4 grains
		Alcohol		½ drachm
		Sweet spirit of nitre		4 drachms
		Distilled water, to make		4 ounces.
136.	℞.	Ergotin		2 grains
		Yohimbine		1/10 grain
		Sodium bicarbonate		2 grains.
		Prepare 20 such doses in capsules.		
137.	℞.	Fluidextract of cimicifuga		18
		Elixir of three bromides		45
		Peppermint water, to make		120.
138.	℞.	Sodii brom		gr. iij
		Acid. acetysalicyl		gr. iij
		Atropin. sulf.		gr. 1/600
		Tr. gelsemii		♏ij
		Cupri sulf		gr. ¼.
		D. t. d. caps. No. xxxvi.		

COMMENTS ON FOREGOING PRESCRIPTIONS

1. Liable to explode, as ammonia combines with iodine, forming the dangerously explosive nitrogen, iodide, NI_3.
2. The spirit of nitrous ether, if acid, is apt to act on the tannin of the uva ursi and froth violently, sometimes exploding the bottle.
3. Don't dispense. Dangerously explosive.
4. Can be put up if mixed cautiously in large open dish.
5. Mass these pills with kaolin and vaselin. Ordinary excipients will cause explosion.
6. This prescription was evidently written with the idea that the fat, petrolatum, would saponify with the calcium hydroxide as would an animal or vegetable fat. It does not do this, and an unsightly mixture results.
7. Chemical incompatibility. Insoluble quinine acetate formed.

8. This mixture turns bluish-green on standing due to the reaction of the oxidase in acacia upon one of the constituents of the tincture of guaiac. Remedy: inactivate the oxidase in acacia by boiling a solution of the gum for twenty minutes.

9. Red ferric hydroxide is precipitated by ammonium carbonate.

10. Unless this prescription is correctly compounded a very unsatisfactory mixture will be produced. First of all, the camphor should be dissolved in the tincture of benzoin. This solution should be added slowly to the mixed acetic acid and rose water and the precipitate which forms should then be removed from the liquid. To this precipitate is added, in a separate mortar, 2 drachms of acacia and to this mixture is then added the liquid little by little, with steady trituration until a homogeneous lotion is formed.

11. When the citrate is dissolved in the water and the spirit of nitrous ether is added, the alcohol of the spirit throws the citrate out of solution. This salt redissolving in the water, the product becomes a two-layered fluid. Remedy: replace half of the water with glycerin.

12. This gave sometimes a clear, water-white solution, sometimes a red precipitate of mercuric oxide, due to reaction between the borax and mercuric chloride; and it would vary even when made up by the same dispenser and with the same materials. It gives an illustration of the law of mass action; the concentration of borax and mercuric chloride are such that a very slight excess of one of the ingredients causes the precipitate to form, the variation observed being probably due to slight differences in the weighing. As confirmation of this, it has been found that with powdered borax a copious red precipitate was always given, the powder having probably effloresced slightly, so that one always got a small excess of borax. If this theory were correct, the presence of one of the products of reaction should alter the equilibrium in the opposite direction, and on adding 30 grains of sodium chloride a perfectly clear solution would be obtained every time, even if powdered borax were used. Increasing the quantity of glycerin to 4 drachms would also generally prevent precipitation (using crystal borax), although a precipitate would form occasionally. This is a good example of the use of glycerin in retarding or preventing chemical action. The lotion in each case was made by dissolving the borax in the glycerin and half the water, dissolving the mercuric chloride in the remaining water (using heat), cooling and mixing the two solutions, and dissolving the potassium chlorate in the mixed liquids.

13. This is all right, affording a good means of administering HCN, this being liberated in the action of citric acid on the potassium salt.

14. Compounded as written, a turbid mixture results, due to the partial precipitation of the glycyrrhizin by the acids of the wine. The addition of a few drops of ammonia water will produce a clear fluid.

15. *Chemical.*—Ammonia in spts. ammon. arom. acts on chloral to form chloroform, which is immiscible.

16. This prescription is apt to produce a turbid mixture. Hilton proceeds as follows: triturate the oils and the creosote with about 10 Gm. Terra Silicea Purificata, U.S.P. XI (Purified Kieselguhr) or purified talcum (coarse powder) until thoroughly mixed. Add 1 ounce of distilled water and filter through a moistened filter paper which has been thoroughly wetted and allowed to drain. When all has passed through the filter, wash with a small amount of water and add simple syrup to make 1 pint. This will make a perfectly clear mixture containing all of the soluble ingredients in the prescription.

17. *Chemical.*—This solution remains clear only when exactly neutral; the bismuth salt being insoluble in acid and the pepsin insoluble in alkaline solution. It being difficult to preserve neutrality, the bismuth citrate is always precipitated in time.

18. *Chemical.*—The calx saponifies the copaiba, just as does magnesia in the formerly official mass of copaiba; in this case, however, to make a creamy emulsion.

19. When this is compounded a clear solution results, but after a few hours a mass of caffeine crystals separate. Scoville points out that it presents a fine illustration of hydrogen-ion concentration and buffer salts. Urotropin (hexamethylenamine) breaks up the loose combination between the caffeine and the citric acid in the citrated caffeine and while this acid would normally attack the urotropin (forming formaldehyde and ammonium citrate) it has weak ionizing power and in the present instance "weak" citric acid is prevented from decomposing the urotropin by the presence of the buffer salts, the acetate and the citrate of potassium.

20. This mixture, while originally brown, becomes colorless by formation of hydriodic acid. It is presumed that the hydrocyanic acid breaks into cyanogen.

21. *Chemical.*—The salt in the bread may react with the silver nitrate to form insoluble silver chloride.

22. Precipitation noted when this prescription is compounded is due to the formation of insoluble codeine iodide. Hydriodic acid and saline iodides have a way of precipitating alkaloids.

23. This is a clearly incompatible prescription as the resin of cannabis will be precipitated by the water. A "shake well" label scarcely fits the case, as the resin comes down in particles preventing equality in dosage. Emulsification with acacia is the proper remedy.

24. *Chemical.*—The carbonate reacts with ferrous iodide, forming insoluble ferrous carbonate, $K_2CO_3 + FeI_2 = 2KI + FeCO_3$.

25. *Chemical.*—The free acetic acid in the Basham's mixture will precipitate insoluble quinine acetate.

26. *Pharmaceutical.*—The bromide, in dissolving, refrigerates the peppermint water, rendering the dissolved oil less soluble and causing excess to separate, making milky mixture. Remedied by dissolving the salt in pure water and adding peppermint water to the required amount.

27. *Chemical.*—The excess of bicarbonate will precipitate the quinine, the resin in the tincture of guaiac will be thrown out by the water. No remedy.

28. *Pharmaceutical.*—Resin of guaiac precipitated by the water. Remedy by emulsionizing.

29. This mixture, upon standing in moderate sunlight, deposited a black mirror on the side exposed to light. When the discolored mixture was placed in the dark, it became white again. Bryant thinks that the blackening was due to the action of the bicarbonate upon the bismuth salt, with some possibility that the oil of peppermint aided in the reaction.

30. This is ear drop formula which has been spoiled through a blunder of the prescriber. Expressed oil of almond, *not* oil of bitter almond was intended.

31. These ingredients mix quietly to a fluid darker than the original constituents. After ten or fifteen minutes however a violent effervescence begins with the evolution of N_2O_4 and other acrid fumes (possibly ethyl nitrite, aldehyde, etc.) and after the effervescence subsides the volume of the fluid is reduced about one-half (evidently due to evaporation of the alcohol of the tincture). The two acids may be mixed without untoward results, but either the alcohol or the iron salt in the tincture starts the trouble. It is obvious that the prescription should not be dispensed as written, since a serious explosion may result after the mixture is bottled and is in the hands of the purchaser.

32. Dispensed as written a heavy precipitate is produced, due to the resin in the liquid extract of hydrastis being thrown down. When the liquid extract of ergot, the tincture of nux vomica and the liquid extract of liquorice are mixed together no precipitate occurs. To the mixture of these three add 1 ounce of chloroform water and 1 ounce of mucilage of tragacanth. Then add the liquid extract of hydrastis and shake quickly, the precipitate produced diffuses readily. Then make up to volume with chloroform water.

33. *Chemical.*—Clear solution is formed by adding the tincture of iron and the solution of arsenous acid to about 3 ounces of freshly prepared Basham's mixture, dissolving the alkaloids in this mixture, adding an aqueous solution of the corrosive sublimate, and finishing with sufficient Basham's mixture to make 4 fluidounces. But the alkaloids are precipitated by the corrosive sublimate on standing, and the mixture is too dangerous to dispense.

34. Both *Chemical* and *Pharmaceutical.*—Tannin precipitates the morphine. Resin of myrrh separated by the syrup. Nothing can be done with it.

35. *Chemical.*—Almost anything is possible. Thus the bichloride separates mercury when combined with the potassium bicarbonate of Fowler's solution; it is incompatible with ferrous iodide and precipitates the alkaloids of the cinchona elixir, while the syrup is incompatible with everything else. As the *Pharmaceutical Era* (from which it is taken) says: "A much more incongruous mixture can hardly be devised."

36. Cocaine or any other alkaloid will be precipitated by the alkaline borax. If boric acid were used, no precipitation would occur.

37. The bichloride and the iodide combine to form potassio-mercuric iodide, an alkaloidal precipitant (p. 901). This will throw the cinchona alkaloids out of solution.

38. The darkening is due to reaction between the alkaline borax in the ointment and the calomel with formation of black mercurous oxide. This is an instance of the objection to borax as an ingredient in Unguentum Aquæ Rosæ of the British Pharmacopœia.

39. It is evidently the intention of the prescriber to use the potassium hydroxide to form water-soluble "soaps" of the resins present in the tincture. Then to further help matters, he included the alcohol. If the orthodox method of handling this mixture is employed, *i.e.*, mixing the alcohol with the tincture and then adding the solution of potassium hydroxide, a clear solution will result at this stage. Now as the cinnamon water is added, a sticky mass of resinous material is thrown out of solution and floats on the top of the mixture. Since the tincture has been diluted by the addition of the

alcohol the potassium hydroxide has not been able to exert its saponifying action, so that on the addition of the water the alcoholic concentration is reduced to such a low point that the resins do not remain in solution.

If, on the other hand, the solution of potassium hydroxide and the tincture are mixed, then the cinnamon water added and, lastly, the alcohol, no difficulty is experienced.

40. *Chemical.*—Incompatible, though often prescribed with good results. Silver salt reduced by vegetable extracts. Dispense by adding a grain of kaolin to each pill and making up with petrolatum. This will lessen likelihood of reduction, although not totally removing possibility.

41. *Chemical.*—The hyposulfite reacts with the precipitation of sulfur and the evolution of sulfurous acid gas. The sulfur precipitates in varying tints, from yellow, through pink, to gray, causing much annoyance in arousing suspicions of the patient. It is to be dispensed, however, as it possesses therapeutic value.

42. In a prescription of this type the average physician intends to prescribe sodium bicarbonate. The British Pharmacopœia dose of carbonate is 5 to 30 grains, but it is generally considered to be too irritating for internal administration, unless largely diluted with water. It was decided by the English dispenser to use bicarbonate.

43. *Chemical.*—The salts effervesce on combining, and a precipitation occurs when the tincture is added. The effervescence is probably due to the following reactions: $K_3C_6H_5O_7 + KHCO_3 + H_2O = K_2HC_6H_5O_7 + CO_2 + 2KOH$. And the alkaline hydroxide precipitates the alkaloids from the tincture. A dangerous mixture that must be dispensed with a "shake" label.

44. In compounding this prescription, if ordinary "fillers" (say powdered licorice) are used a large amount of the powder must be used and a 10-grain pill will result. The addition of 1 grain of wax and ½ grain of heavy magnesium oxide to each pill will produce a product which, in the first place, will be small in size, and in which the ingredients will be uniformly divided, permitting no leakage of the oil.

45. This ear-drop prescription, now popular in England, upon standing becomes irritating to the ear passages due to the oxidation of the alcohol producing as much as 1 per cent of acetic acid and about 0.5 per cent of acetaldehyde. The mixture should be kept in a cool dark place to lessen the degree of oxidation.

46. Triturates to pasty mass, due to the 60 per cent water in the official crystalline sodium phosphate. Best remedy is that of using exsiccated sodium phosphate, 1¼ ounces, and sugar of milk, 1¼ ounces.

47. Hilton's method of procedure follows: dissolve the mercury oxycyanide in water in a wide-mouth jar, add the glycerin, mix and add the tragacanth. Allow the mixture to stand until a smooth jelly is formed, strain through muslin and add the oil of lavender. Dispense in ointment jar.

48. The acid will be largely dissolved by the alkaline solution of ammonium acetate. There is a possibility that the salicylic acid may react on the spirit of nitrous ether, especially if it is acid. Kaemmerer filtered out excess of salicylic acid, a procedure not approved by most of those who discussed the prescription; one gentleman suggesting that enough ammonia water be added to insure complete solution.

49. In compounding this prescription, according to Dr. Hilton, oxyquinalone sulfate should be used. Chinosol is a trade-marked brand of oxyquinalone sulfate.

The only way to make clear solution of the above is to dissolve each salt separately in about 90 cc. each of water and render the resulting solutions slightly alkaline in each case with solution of sodium hydroxide. Then mix the two solutions and if the resulting product is not entirely clear, add a few more drops of the alkali solution.

50. This, according to Hilton, is a dangerous prescription. The tannin in the digitalis reacts with the iron, forming tannate of iron, and there is possibly some action that would decompose the constituent glucosides of digitalis. The finished product might be suitable for writing a death certificate.

51. Hilton points out the irritating properties of this chemical which is apt to produce eczematous eruptions upon the fingers of the compounder of the prescription. Remedies: wear rubber finger cots, fill the chemical into No. 4 capsules and clean the filled capsules thoroughly with absorbent cotton. Then slip the cleaned capsules into No. 3 capsules and dispense.

52. If carelessly compounded, the ferric pyrophosphate will be precipitated by the acid. If the pyrophosphate is dissolved in 3 fluidrachms of hot water, the syrup then added, and lastly the acid, little by little, shaking after each addition, a clear solution results. The dispenser used Diluted Metaphosphoric Acid N.F. III, (p. 453) instead of the official diluted phosphoric acid.

53. This prescription should be compounded as follows:

(*a*) Prepare a saturated solution of zinc sulfate, 2 apoth. ounces, in distilled water to make 2 fluidounces.

(b) Dissolve 2 apoth. ounces of sulfurata in distilled water to make 2 fluidounces and filter.

Mix solutions "a" and "b" and stir until effervescence ceases. Dissolve the beta-naphthol in the alcohol, triturate with the sulfur and to this add the sulfide mixture with constant trituration until 4 fluidounces of fluid is obtained.

54. If this prescription is compounded as written a thick heavy sediment is formed which it is impossible to remove from the bottle. The correct procedure is to use, in place of the tannic acid, 20.0 of glycerite of tannin. The alum is first dissolved in the Dobell's solution and the glycerite of tannin is added a little at a time. By this procedure a fine clear solution will be obtained. There is no objection to the glycerin of the glycerite of tannin. Glycerin is present in the Dobell's solution and the additional few cubic centimeters which are added will not have the slightest effect on the therapeutic action of the finished prescription.

55. *Chemical.*—The arsenous acid of Fowler's solution produces, with tincture of ferric chloride, insoluble ferric arsenite.

56. *Chemical.*—The ammonia will precipitate the quinine from the scale salt solution.

57. This prescription, according to Dr. Hilton, cannot be dispensed as a clear solution. Sodium bicarbonate is soluble 1 part in 20 parts of water. The prescription contains only about one-half the amount of water necessary to dissolve the sodium bicarbonate. Compounded in the ordinary way the liquid will darken on standing; this is due to reasons given on p. 492.

58. *Chemical.*—A popular lotion that must be dispensed with a "shake" label. Lead meconate precipitated.

59. This prescription cannot be compounded as written since argyrol does not dissolve in oils and fats. The remedy, according to Lascoff is to dissolve the silver protein in a minimum amount of water, to mix this with a small amount wool-fat and to incorporate this mixture with the albolene.

60. *Chemical.*—The quinine will not entirely dissolve, there being an insufficient amount of acid in the tincture to accomplish the purpose. Add a few drops of hydrochloric acid.

61. *Pharmaceutical.*—The usually insoluble quinine salt will, under the influence of antipyrine, dissolve in the small quantity of water directed in the above prescription, forming what is called "chinopyrine," which affords a good method of administering quinine hypodermically.

62. *Chemical.*—Dangerous, as corrosive sublimate is formed by the following reaction: $3Hg_2Cl_2 + H_2O + 2C_{11}H_{12}N_2O = 2Hg + Hg_2O + 2HgCl_2 + 2C_{11}H_{12}N_2OHCl$.

63. The strontium bromide reacts with the sodium citrate present in the elixir of gentian with the formation of strontium citrate, which precipitates. The alkaline Fowler's solution precipitates alkaloids hence there is some danger of reaction with the alkaloids of the tincture. However in this case the amount of Fowler's solution is so small, that there is not much chance of serious results. On the other hand, in England a fatality occurred through the dispensing of equal quantities of Fowler's solution and solution of strychnine.

64. Ferric chloride liberates iodine from the iodide.

65.—An impossible combination, according to Dr. Hilton, since the sweet spirit of nitre reacts with the amidopyrine to produce aniline colors and an unsightly liquid. The only remedy is to omit the sweet spirit of nitre and this should be done only with the consent of the prescriber.

66. This prescription produces a "shake well" mixture. Moreover, to produce a uniform preparation, finely powdered drugs should be used and the mixture should be washed through fine muslin.

67. This is a case of chemical incompatibility. Dobell's solution contains 15 Gm. of sodium borate in 1000 cc. This acts on the zinc chloride and there is formed zinc borate, a complex insoluble salt. Zinc salts cannot be mixed with anything containing borax.

68. This illustrates the well-known incompatibility of acetylsalicylic acid with sodium bicarbonate. The dispenser placed each of the three ingredients into the capsule separately; the bicarbonate in the center. Hilton considers the prescription, even when so dispensed, as dangerous since irritating quantities of salicylic and acetic acid will be produced in the stomach.

69. To produce a solution, the alkaloid cocaine must be employed, since cocaine salts do not dissolve in liquid petrolatum. In compounding such prescriptions, oleate of cocaine, U.S.P. VIII, comes in handy.

70. This and the five prescriptions which follow were published by H. A. B. Dunning. The ointment prepared by recipe, No. 70, when rubbed on the skin separates into greasy liquid and quill-like masses. If the balsam is mixed with an equal volume

of alcohol and rubbed with an ointment made of the petrolatum and the other ingredients a satisfactory product is obtained.

71. Although solutions of bicarbonates and solutions of soluble magnesium salts are incompatible, the reaction takes place but slowly. The compounding of this prescription results in a perfect solution in which carbon dioxide is slowly but gradually liberated. After several hours the mixture becomes cloudy and finally a precipitate is formed. The more rapidly the carbon dioxide is allowed to escape the sooner a precipitate forms; this is because the carbon dioxide serves to keep the otherwise insoluble magnesium carbonate in solution.

72. This mixture is persistently effervescent, due to separation of the ethyl nitrite from the spirit by action of the water of the syrups; the separate ethyl nitrite boiling at ordinary temperatures.

73. Camphor and salol liquefy in contact with each other and if the ingredients of this prescription are mixed as written, a paste results which requires a large quantity of absorbent powder to properly stiffen for dispensing in capsules. It cannot well be dispensed in soft elastic capsules. Dunning dispensed the prescription as follows: pack the salol into ten No. 5 empty capsules. Mix the other ingredients and pack loosely into ten No. 1 empty capsules. Into the No. 1 capsules insert the No. 5 filled capsules so as to conceal the latter.

74. The potassium chlorate and sodium hyposulfite should be powdered separately and mixed lightly to avoid an explosion.

75. In dispensing this, powder the menthol and pack into thirty No. 5 capsules. Mix the other ingredients and place into the lower halves of thirty konseals. Put a menthol capsule in each and proceed as usual.

76. This mixture, which with the two which follow were submitted by Peter Fenton, gives a white precipitate soon after making up. The precipitate is lead citrate. It may be assumed that the prescriber's intention here in adding syrup of lemon is merely for flavoring. By using simple syrup, to which some tincture of lemon has been added, instead of syrup of lemon the formation of the insoluble lead salt is prevented.

77. In this case precipitation is prompt and the deposit abundant. The precipitate is due to the sodium borate throwing out the alkaloids. As written, no attempt should be made to dispense the above. (See No. 36.)

78. These ingredients, when mixed produce an attractive green solution, due to the formation of citrochloride of iron.

79. The compounded prescription became yellow and finally deposited a yellow sediment of iodoform; due to the fact that ether in the presence of air and water converts some of the latter into hydrogen dioxide and this oxidizing agent liberates iodine from the iodide.

80. In this, ammonium chloride is formed, formaldehyde is set free and ferric hydroxide is precipitated.

81. In compounding this prescription, Tait found that the liquid became yellow and then brown, due to liberation of irritating free iodine. Experiments showed that the addition of minute amounts of sodium hypophosphite even as little as ½ grain to a fluidounce of the mixture—prevented liberation of iodine. A lesser amount of the hypophosphite—say 1/16 grain to the fluidounce—prevented darkening of the mixture when kept protected from the light, but when exposed to sunlight the liquid turned brown. Curiously, if the mixture was then put in a dark place it bleached and the alternate darkening and bleaching, according as to whether it was in the sunshine or out, could be repeated again and again.

82. When this is compounded, there are deposited crystals of potassium sulfate which are less soluble in water than is sodium sulfate and in this mixture is still less soluble because of the presence of the alcohol in the spirit of nitrous ether.

83. Discussing this prescription, the anonymous author states that it is reminiscent of the story of a well-known doctor-cricketer who, when acting as house physician, was called to account by the hospital pharmacist for prescribing something in the "blue-black" line, and was rather curtly asked "if he desired his patient to take ink"? The doctor was not so ignorant as was supposed, for his reply was brief and to the point: "As ink is official in the British Pharmacopœia (mist. ferri aromat., B.P., '85), he failed to see the purport of the dispenser's query, and he certainly desired his patient to take ink."

84. Dispensed as written an unsightly and unsatisfactory mixture is produced. This is due to the unstable acidity of the caffeine salt. By substituting the equivalent quantity of caffeine alkaloid for the citrate prescribed, a clear mixture is presented, and, at the same time, the therapeutical intentions of the prescriber are maintained.

85. This prescription may be compounded in the following fashion: dissolve the phosphorus in a sufficient quantity of carbon disulfide; place 20 grains of wool-fat in a mortar, add the solution of phosphorus and stir until the mixture is liquefied; then add

the other ingredients, make into pills and coat with sandarac varnish or some similar protective coating.

86. The incompatibility is due to the precipitation of some of the salicylic acid of the salicylate by action of the hydrobromic acid. Finnemore and Gorringe find that by the use of 60 grains of potassium citrate as a buffer salt, precipitation is prevented.

87. This prescription may be compounded as follows: triturate the iodine and potassium iodide with a small quantity of water and mix the solution with a portion of the lard. Thin the soft extract of belladonna with a few drops of water, mix with the remainder of the lard, and incorporate the two portions.

88. This prescription produces a milky mixture due to the precipitation of the ephedrine as an iodide.

89. This English prescription upon compounding produces a copious precipitate. When glycerin of borax and glycerin of tannic acid with water or alum in solution and glycerin and tannic acid are mixed, there is no precipitation in either case. When alum in solution and glycerin of borax are mixed together there is a slight precipitation. When alum in solution, glycerin of tannic acid, and glycerin of borax are mixed together the copious precipitate mentioned above is thrown down. This appears to be the aluminum boro-tannate mentioned by Martindale, and known also as Cutol.

90. According to LaWall, this prescription is faulty, since the production of a perfect solution requires the use of eight and one-half times the amount of sodium chloride you have of iodine. This prescription will require 1 ounce of sodium chloride. Further, it is necessary to use C. P. sodium chloride because ordinary table salt usually contains starch, calcium carbonate or magnesium carbonate. Starch will produce a blue color; the other two salts are not satisfactory.

91. The best way to dispense this prescription is to melt the cacao butter and the almond oil, then dissolve the resorcin in a few drops of water and rub it up thoroughly with the precipitated sulfur; then rub the rest of the ingredients on a slab, little by little with the melted cacao butter, until it forms a nice, smooth, perfect ointment.

92. This prescription looks very simple, but the prescriptionist will be surprised to find that when he rubs the two ingredients together, they form a gritty, hard ointment, which is absolutely impossible to apply to any sore. Lascoff found that a few grains of powdered acacia added to the balsam of Peru and mixed with the zinc ointment, will form a smooth, soft ointment.

93. This mixture is likely to explode after standing an hour or two.

94. Protargol like most silver salts is precipitated by chloride, so the dispenser used the proportional quantity of cocaine nitrate and a clear solution resulted.

95. In combining the ingredients as written, a damp powder results, gradually becoming semiliquid. This can be overcome by replacing half the citrated caffeine with the caffeine alkaloid (in order to adjust the strength), adding heavy magnesium oxide, 1 grain to the capsule, combining the latter with each ingredient separately and finally mixing all to form a uniform powder.

96. According to Morrison, if the epinephrine solution is placed in a bottle, the resorcin and antipyrine dissolved, and the normal saline solution then added, as is usual an oily substance will separate. A reaction takes place between the resorcin and the antipyrine forming this oily liquid which settles in the bottom of the bottle. However, a perfectly clear solution is obtained if each of these drugs is dissolved separately in some of the normal saline and then mixed.

97. This mixture should never be dispensed, as Cushny and other authorities report that the filicic acid in the oleoresin dissolves in the castor oil and being absorbed, produces blindness.

98. Sodium nitrite gives trouble owing to the ease with which it is decomposed with liberation of oxides of nitrogen. The mass is also apt to crumble, possibly due to coarse particles in the digitalis. By using anhydrous wool-fat a nice mass was obtained without any change of color or odor of oxides of nitrogen. Care should be taken that the wool-fat is not acid.

99. This prescription (Fig. 290) seems an impossible one, since it is well known that permanganate and oxalic react with mutual decomposition. The physician however insisted he wanted it as written, so Dr. Lascoff triturated *very cautiously*, the permanganate and the oxalic acid with water and then mixed the resulting manganese dioxide with the iron salt previously made into a mass with kaolin and petrolatum.

100. Hilton suggests the following compounding of this prescription: dissolve the acetanilid in the alcohol and add the aromatic spirit of ammonia; dissolve the sodium phosphate in the water with the aid of gentle heat and add the sodium bromide; cool and mix the two solutions. This makes a slightly milky solution due to the aromatic spirit of ammonia. If a clear solution is desired filter the mixture through paper with the aid of a small amount of Kieselguhr.

101. According to Nichols, when this prescription was first prepared, it was cloudy because of the separation of the spirit of chloroform, but in time the chloroform would settle to the bottom of the container. This separation may be overcome by using aromatic elixir, which gives a clear preparation.

The physician has tried to get something that is palatable, and the difference between the elixir and the aqueous combination does not alter the intention of the prescription. Saalbach, in discussing this prescription, prefers using some alcohol instead of aromatic elixir.

102. This prescription, presented by Morrison, causes one to wonder just what purpose it is intended for and its composition should put the pharmacist on the alert for an incompatibility. A grayish colored precipitate formed which was too heavy to be held in suspension. The potassium iodide reduced the calomel to mercurous oxide and metallic mercury. Furthermore, all the sodium citrate would not dissolve, in the prescribed vehicle. Substitution of water for the elixir is not advisable for the vehicle also contains one of the active therapeutic constituents. Such a mixture should not be dispensed, as written; in this case, after conferring with the physician, the calomel was omitted from the prescription and the amount of sodium citrate was reduced.

103. This represents an old-time combination of alkaloids of hydrastis and of opium precipitated by borax. According to Nichols, there is no particular need for the borax and it can either be omitted entirely or replaced by the proper amount of boric acid. This is one of the prescriptions that a pharmacist really should not dispense as it is, because the alkaloids settle to the bottom of the container. If the preparation is shaken up there is a fine suspension but it still has a cloudy appearance; and, of course, we try to dispense preparations always in a clear condition and make as elegant a pharmaceutical product as possible.

104. Iodides, bromides, tannates and benzoates form insoluble salts with alkaloids, and therefore as a rule they are not prescribed together except in some formula, which has shown to be satisfactory.

105. The product made by this prescription turns brownish-gray on aging. The trouble is with the resorcin. In mixtures or on exposure it darkens. Hilton proceeds as follows: use heavy oxide of magnesia, mixing this intimately with the oil of peppermint and the calcium carbonate in a mortar; transfer the mixture to a slab; reduce the resorcin to a fine powder and sprinkle same on the mixed powders, triturating lightly until mixed; dispense in glazed papers.

106. This is a classic prescription that has been given in textbooks on pharmacy for the past fifty years. It figures in one of the fascinating detective stories of Agatha Christie. In the days when English pharmacists brought it to light, the average medicinal potassium bromide contained a considerable excess of free alkali; the bromide of today contains very little alkali. Kremers points out that the precipitation, if any, may be due to the alkalinity of the glass container. Anyway, the old idea of the precipitation of crystals of strychnine bromide has to be dropped.

107. This prescription for an eye lotion is defective, since precipitation occurs. The precipitate consists of zinc borate. As eye drops should not contain solid particles this prescription should be revised by the prescriber.

108. On the face of it this prescription looks impossible, because of the presence of the alkaloid and of free acid with potassium iodide. But the mixture can be dispensed successfully, in the following manner: dissolve the quinine salt in the smallest possible amount of acid, say ¾ minim to each grain (so as to have the smallest possible amount of free acid present). Then dilute the solution with half the vehicle. The iodide is dissolved in the other half of the vehicle and having then diluted the two salts to the utmost, bring them together.

109. Ammonium valerianate is very hygroscopic and as a result a semifluid is formed. Add powdered althea to form a mass and make pills as directed.

110. To avoid liberation of iodine and formation of a precipitate of iodosulfate of quinine in course of time, Wyatt dissolves the quinine in sufficient hypophosphorous acid and adds it to the mixture after dissolving the iodide in the syrup.

111. This prescription was compounded as a good-appearing well-diffused mixture by emulsifying the thymol with 2 drachms of acacia plus water and then adding it to a solution of the other ingredients.

112. As the extracts of chamomile and gentian are quite soft, a soft pill mass will result. Knott prepares a suitable mass by the following procedure: place the two extracts just mentioned in a flat-bottomed capsule and dry them as far as possible on a water bath. Shred 12 grains of wax, melt it, and add to the oil of caraway, then the powdered asafetida and the dried extracts. A little licorice powder may be required to complete the mass.

113. If this prescription is compounded with chemicals which are free from impurities a clear solution should result. If, however, impure chemicals are used in compounding

a precipitate may form. Should this happen some pharmacists would add powdered acacia to the mixture. Here, again, the question of *purity* arises. If the acacia is not of a high grade quality it will have an effect on the color and the appearance of the mixture. The correct method is to compound and dispense this prescription without the addition of any acacia.

114. Hilton's method of compounding this prescription is as follows: dissolve the menthol in 1½ ounces of alcohol, add the sulfur and mix thoroughly; dissolve the resorcin in the rose water and then add the alcoholic mixture and enough rose water to make 16 ounces.

To obtain a smooth mixture where sulfur is directed it is necessary to use sufficient alcohol to suspend the sulfur; otherwise it will be lumpy and float on top of the mixture.

115. This "ear-drop" prescription may be compounded by dissolving the camphor in the phenol with gentle heat; then adding the glycerin and lastly the water.

116. This prescription had been dispensed as a milky suspension, but when refilled by another pharmacist a solid mass deposited in the bottle. It appears that the magnesium carbonate is the troublesome ingredient. Morrison suggests that there would be no difficulty if the sodium bicarbonate be dissolved in some of the peppermint water, the glycerin and phenol added and, finally, the magnesium carbonate, with thorough shaking.

117. To avoid acidity and the consequent liberation of nitrous acid from the nitrite and the certain production of varying amounts of iodine from the iodide, Wyatt adds 20 grains of sodium bicarbonate to the mixture, and the nitrite last.

118. This prescription was compounded by dissolving the salts separately, and then mixing. A clear solution resulted but on standing a few minutes a white precipitate formed. Hilton points out that theobromine-sodium salicylate decomposes quickly when exposed to air and becomes insoluble. A few drops of 5 per cent solution of sodium hydroxide will render it soluble. Ammonium chloride is incompatible with theobromine-sodium salicylate and the prescription cannot be dispensed as a clear solution.

119. Compounded as written, a thick precipitate is formed, which on standing becomes hardly diffusible. This is due to the action of the hydrochloric acid on the extract of licorice with precipitation of glycyrrhizin. Rub up 1 drachm of compound tragacanth powder with some of the infusion to form a mucilage, and add with shaking the extract of licorice and tincture of nux vomica. Dilute the acid with the remainder of the infusion and mix the two liquids. The precipitate diffuses well on shaking.

120. Time and again this and similar prescriptions have caused pharmacists considerable trouble, which is due entirely to the wrong method of incorporating the balsam of Peru. In this prescription the balsam of Peru should be mixed with the petrolatum and then the iodoform should be added in small portions at a time. If the iodoform and the balsam of Peru were mixed first, the gummy portion of the balsam would immediately separate and its inclusion would be impossible.

121. Stedem adds a drop or so of water to the extract, mixes this dilution with the ichthyol and with half of the oil of theobroma to a workable mass. He mixes the tannin with the rest of the oil of theobroma, adds it to the ichthyol mass, brings the mixture to the fusion point and pours into chilled molds.

122. The compounded prescription after standing twenty-one days in a warm room exploded. As Hilton says, this is a good example why screw-cap bottles should not be used for prescriptions. If it had been a cork-stoppered bottle the cork would have blown out and no further trouble would have been had. The explanation is easy. Calcium lactate is slightly acid. The finished prescription contains about 8 per cent of syrup or about 4 per cent sucrose. The slight acidity of the mixture from the calcium salt and in a warm room changed the sucrose to invert sugar. This readily ferments at room temperature, forming alcohol and carbon dioxide. As the screw-cap could not blow off, the bottle could not stand the pressure.

123. This ointment was prepared by Hilton as follows: melt the white wax at a low temperature and add anhydrous lanolin, stir until melted and add the liquid petrolatum, transfer to a warm mortar and gradually add the citric acid previously dissolved in distilled water and heated to the same temperature as the first mixture; stir briskly until cold and then add the oil of lemon.

124. This prescription upon compounding furnished solutions having colors varying from yellow to bright red. Hilton points out the mistake of prescribing sweet spirit of nitre in combination. It should be used alone. However, when in combination it is necessary to first determine whether it is neutral or acid. If acid it should be rendered neutral with potassium bicarbonate. Evidently the spirit of nitre had become acid on standing and possibly the syrup of tolu (nitrogen tetroxide being liberated) produced the red color.

125. This mixture darkens on standing, due possibly to the acidity of the mucilage of acacia, which breaks down the creosote carbonate. If the mucilage of acacia is neu-

tralized with a little ammonia water and if the syrup of tolu is not acid, there will be no change in color of the mixture.

126. Prescriptions of this type and especially those that contain additional resinous matter, have a tendency to lump, stick to the sides of the container and fail to be homogeneous. Three or four grains of tragacanth per ounce will work wonders toward the dispersion of the ingredients of such preparations and prevent the settling down into a hard mass of a dense substance which cannot be shaken loose after standing for some time. The British practice of using compound tragacanth powder for dispersion purposes might well be copied in this country. Its small starch content helps decidedly for obstinate cases of this kind. The judicious use of mucilage of acacia where no heavy ingredients are present is frequently all that is necessary, if small amounts of glycerin or syrup do not serve the purpose.

127. Several days after filling the prescription, the pharmacist learned that it had turned dark and the taste had changed. It looked as though charcoal had been added. Hilton points out that as the magma of bismuth is alkaline, a decided action on the tinctures took place with a corresponding darkening. The action is slow. No doubt some of the bismuth hydroxide was changed by constituents of the tinctures and certain gums were precipitated. There seems to be no way to overcome the difficulty in this combination.

128. It was reported that after two or three days, this prescription showed signs of precipitation. Hilton finds that the trouble is due to fungus growths. The only remedy is to sterilize the solution before sending it to the patient.

129. Wyatt points out that this is a very dangerous preparation. It was applied to a glandular swelling in the neck, but proved so severe that its use had to be stopped. Iodide of mercury was formed, and this in a practically nascent condition penetrated the skin so deeply that severe blistering was caused. Sometimes external and internal treatment when administered simultaneously may prove therapeutically incompatible.

130. When the solutions of the calcium and sodium salts are mixed a precipitate of calcium sulfate results. There is no way to remedy the trouble.

131. Upon standing, the compounded prescription deposits a precipitate of calcium citrate. The only remedy would be to request the physician to prescribe sodium bromide.

132. A flocculent precipitate of magnesium phosphate is formed. No remedy is available except a recasting of the prescription.

133. Since both the salts are water-soluble, no difficulty would be expected with such a formula. On actual compounding, however, it was found that the ordinary procedure of placing the salts into a bottle and filling up with water could not be followed. Nor could one salt be first dissolved in part of the water and the second salt added to this solution; in the latter procedure the second salt lumped rather badly and failed to go into solution within a reasonable length of time; this may be explained—since the first solution is nearly saturated, the second salt is not nearly so soluble in that solution as in water. Terry dissolved one salt in half the peppermint water, and the second in the other half, and then mixed the two solutions; then no further difficulty was experienced.

134. If filled exactly as written, it is a "shake mixture" as the acetanilid is not soluble in the amount of syrup called for. Hilton dissolves the acetanilid in 1½ drachms of alcohol and adds 4 drachms of syrup of orange. He then dissolves the other ingredients in 2 ounces of syrup of orange and mixes the two solutions and then adds enough of the syrup to measure 3 ounces.

135. This prescription is incompatible and cannot be satisfactorily compounded. Sodium hyposulfite is insoluble in alcohol. Solutions of sodium hyposulfite deposit sulfur on standing. Sodium hyposulfite decomposes spirit of nitrous ether, liberating an oxide of nitrogen, a greenish-yellow gas, giving the color. Spirit of nitrous ether should never be dispensed in combination because it decomposes when mixed with almost anything. Even on mixing with water, part is lost before it can be taken. Ethyl nitrite (nitrous ether) boils at 17° C., becomes acid on keeping, decomposes by air, light, heat and moisture.

136. There was no difficulty in preparing the capsules called for in this prescription but after standing several days many of them exploded. Kern believes that the reaction is due to the action of the trace of acid in ergotin upon the bicarbonate.

137. Compounding of this prescription as written produces a preparation having a murky, unsightly precipitate at the bottom of the bottle due to separation of resins and other material.

The addition of 30 grains of powdered acacia in making this mixture solves the problem. Due to possible gelatinization of the acacia by the alcohol present, care must be taken. A mucilage should first be made with the acacia and a portion of the peppermint water, and the fluidextract added, a little at a time. Add the balance of the peppermint water and the elixir. The resulting product is a fine, homogeneous mixture with no precipitation.

138. This is another case where the original white capsules change color on standing. To remedy the situation, Hilton advises the use of an equivalent amount of extract of gelsemium instead of the tincture, the use of the equivalent amount of carefully exsiccated copper sulfate and of carefully dried samples of the bromide and of the acetylsalicylic acid.

DISPENSING THE FINISHED PRESCRIPTION

A chapter could be written upon this important phase of the dispensing art and in truth considerable has been written on the subject in the preceding pages. Thus in Chapter XVIII (pp. 310–313) the dispensing of powders and pills and the wrapping of packages is discussed at some length. Recently, much attention has been paid to attractive glass containers and at this place a few pictures of modern glass prescription bottles are given (Figs. 295–298). Gradually the time-honored cork stoppered bottles are being replaced by metal-capped bottles and by composition

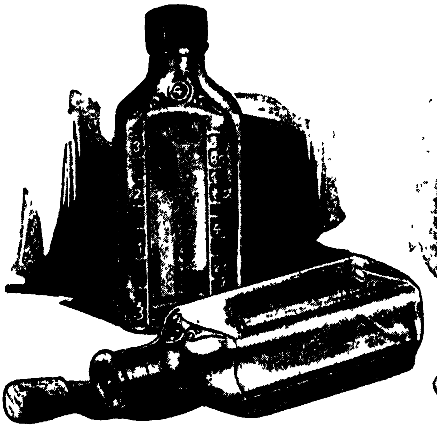


Fig. 295.—Screw cap and cork stoppered prescription bottles. (Courtesy of Owens-Illinois Glass Co., Toledo, Ohio.)

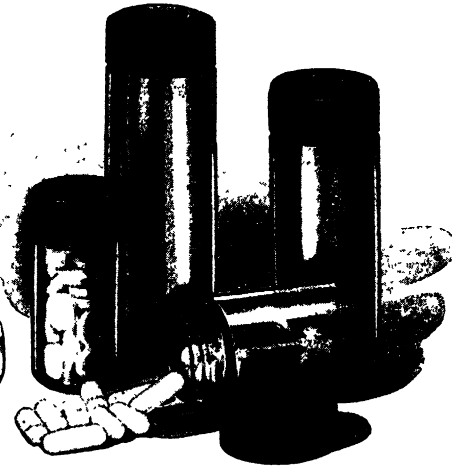


Fig 296.—Capsule and tablet vials. (Courtesy of Owens-Illinois Glass Co., Toledo, Ohio.)

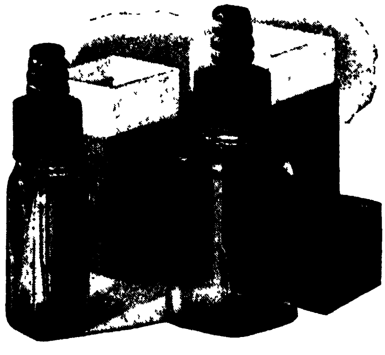


Fig. 297.—Dropper bottles with carton for dispensing eye drops and potent liquids. (Courtesy of Owens-Illinois Glass Co., Toledo, Ohio.)

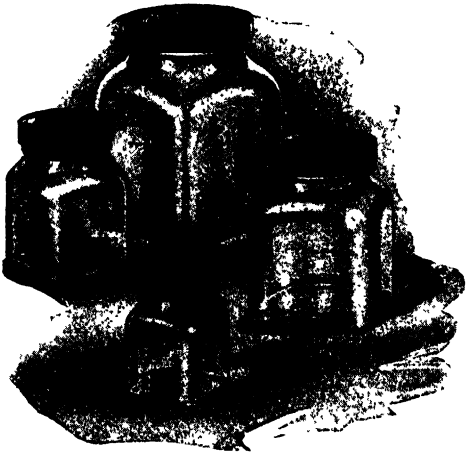


Fig. 298.—Wide-mouth containers with screw caps for dispensing powders. (Courtesy Owens-Illinois Glass Co., Toledo, Ohio.)

screw caps. Hilton and other authorities on elegant and safe dispensing point out that liquid prescriptions that are liable to effervesce should always be dispensed in cork-stoppered bottles; since the evolution of a gas in a screw-capped bottle is likely to cause an explosion, whereas, when a cork stopper is used the extra pressure will be relieved by the blowing out of the cork. In using a screw-capped bottle the cap should be screwed down firmly, to prevent leakage, but not so tight to require the use of gas-tongs by the purchaser.

Most high-grade prescriptionists finish off their liquid medicines dispensed in cork-stoppered bottles with suitable caps. Attractive paper caps fitting each size of cork and bottle are readily obtainable. Caps made from viscose or cellophane (p. 703) are also available.

Bottles used for prescriptions should be comparatively free from alkali and must obviously be scrupulously clean. Modern prescription bottles are usually furnished by glass manufacturers in almost sterile condition.

Colored glass containers are now popular from the esthetic standpoint. The only colored bottles that really protect the medicaments from the deteriorating influence of light are those made from amber glass.

Eye washes should be dispensed in special bottles provided with a dropper. Combinations of the bottle and the dropper in a suitable cardboard container are obtainable from dealers in druggists' sundries.

Some years since, bottle manufacturers featured prescription bottles graduated in the outside in our ordinary and metric units. As investigation indicated that these graduations were notoriously inaccurate, the use of such bottles are prohibited in some States.

Ampuls, sealed glass containers designed for individual doses of medicaments, are described in Chapter LII (p. 988).

BIBLIOGRAPHY

Incompatible Prescriptions.—Kaemmerer, Am. Dr., 47, 1905, 287; McEwan, Pract. Dr., **26,** 1909, 169; Merck's Rep., 19, 1910, 166 and Am. Dr., 58, 1911, 145; Wyatt, Am. Dr., 57, 1910, 337; Elliot, Merck's Rep., 20, 1911, 101; Lemaire, Sch. Wsch. Ch. Ph., **51,** 1913, 91; Dunning, Pract. Dr., 26, 1909, 244 and Bull. Phar., 24, 1910, 290; Fenton, Nat. Dr., 39, 1909, 185; Lascoff, Pract. Dr., 28, Aug., 1910, 41 and Pharm. Era, 44, 1911, 20; Duncan, Merck's Rep., 19, 1910, 224; Anon., Nat. Dr., 40, 1910, 377; Tait, Merck's Rep., 19, 1910, 197; Anon., Brit. and Col. Dr., 1915, 361; Arny, Dr. Circ., 58, 1914, 213; Gilmour, Ph. Jl., 96, 1916, 43; Hill, Ph. Jl., 96, 1916, 397; Griffith and Nichols, Jl. A.Ph.A., 9, 1920, 515 and 979; Lascoff, *ibid.*, 9, 1920, 153 and Dr. Circ., 67, 1923, 265; Tait, Ch. and Dr., 93, 1920, 1773; Kitchen, *ibid.*, 92, 1920, 420; Andrew, Ph. Jl., 107, 1921, 542; Bryant, *ibid.*, 107, 1921, 232; Nobel, Ch. and Dr., 94, 1921, 151; Scoville, Bull. Pharm., 36, 1922, 418; Nichols and Nebinger, Jl. A.Ph.A., 53, 1924, 344; Lincoln, Bull. Pharm., 39, 1925, 168; Kern, Pract. Dr., 44, Sept., 1926, 25; Kremers, Jl. A.Ph.A., 16, 1927, 840; Nichols, Bull. Pharm., 42, 1928, 725; Terry, Jl. A.Ph.A., 17, 1928, 1115; Stedem, Drug. Bull., 51, June, 1929, 27; Dunn, Jl. A.Ph.A., 18, 1929, 66; Peacock, *ibid.*, 18, 1929, 692; Lascoff, N. W. Drug., 37, Feb., 1929, 17; Dr. Circ., 74, Aug., 1930, 16; *ibid.*, 73, June, 1929, 236; Wyatt, Pract. Dr., 47, Dec., 1929, 38; Krantz, Jl. A.Ph.A., 18, 1929, 1153; Loganathan, Pract. Dr., 48, June, 1930, 23; Knott, *ibid.*, 49, Oct., 1931, 43; Hilton, Am. Dr., 84–88, Aug., 1931 to July, 1933 (each month); Osol, *ibid.*, 88–90, Aug., 1933 to Dec., 1934 (each month); Anon., *ibid.*, 86, Oct., 1932, 42; Carruthers, Ph. Jl., 128, 1932, 284; Chamberlin, Ohio Dr., 8, Nov., 1932, 14; Lascoff, Jl. A.Ph.A., 22, 1933, 970.

Glass Containers.—Anon., Merck's Rept., 20, 1911, 146; Jennings, Stand. Rem., 15, Feb., 1928, 28; Husa, Glass Cont., 7, Dec., 1928, 9; and Jl. A.Ph.A., 19, 1930, 159; Partridge, Jl. Ind. Eng. Ch., 21, 1929, 638; Ubrig, Apoth. Ztg., 45, 1930, 1186; Raubenheimer, Merck's Rept., 39, 1930, 154; Newton, Jl. A.Ph.A., 19, 1930, 168; Kroeber, Ph. Zt., 76, 1931, 1165; Arny and co-workers, Jl. A.Ph.A., 20, 1931, 1014 and 1153; *ibid.*, 23, 1934, 672.

1943 SUPPLEMENT

TO

PRINCIPLES OF PHARMACY

(FOURTH EDITION)

By

HENRY V. ARNY

And

ROBERT P. FISCHELIS

W. B. SAUNDERS COMPANY
PHILADELPHIA AND LONDON
1943

PREFACE

This 1943 supplement is being offered with the full realization of the fact that it is not a completely satisfactory substitute for a revised edition of Principles of Pharmacy. Under normal conditions, the authors would have revised the book completely to conform to the new editions of U.S.P. XII and N.F. VII, but owing to illness of the senior author and the fact that the junior author is serving as Chief of the Medical and Health Supplies Section, Office of Civilian Supply, of the War Production Board, such complete revision is impossible at this time. It is hoped, however, that with the issuance of this new supplement, Principles of Pharmacy will prove of value to students and other users of the book

The fourth edition of Principles of Pharmacy was prepared to conform to the U.S.P. XI and the N.F. VI. These volumes became official on June 1, 1936. The U.S.P. Convention of 1930 authorized the issuance of supplements, and the publishers of the National Formulary likewise authorized the issuance of correction sheets and supplements The same procedure has been followed in connection with U.S.P. XII and N.F. VII.

The 1939 supplement to Principles of Pharmacy was prepared and published to bring the fourth edition up-to-date as of January 1, 1940. Since then, the U.S.P. XII and the N.F. VII have appeared, both becoming official on November 1, 1942. Since the demand for Principles of Pharmacy has continued, especially on the part of the Armed Services and students, it was deemed advisable to issue this 1943 supplement embodying information on the additions to the U.S.P. XII and the N.F. VII and carrying such corrections of the text of the fourth edition as will bring this edition into conformity with the new U.S.P. and N.F. standards.

In preparing this supplement, the authors have followed the general plan of Principles of Pharmacy in that the new monographs present condensed pharmacopoeial information with comments designed to aid the student and practitioner to quickly grasp the more important facts about the drugs or preparations under discussion.

Many pharmaceutical preparations are given trade names which indicate proprietorship on the part of a certain producer. The inclusion of proprietary or trademarked titles in the various monographs in this book is for informational purposes and is not to be taken as an indication of the specific standards to which any official or unofficial drug may conform.

Following consideration of the new additions to the official drugs, there are references to the more important changes in the text of Principles of Pharmacy necessitated by changes in the text of the U.S.P XII and N.F. VII authorized by the respective Revision Committees.

Acknowledgment is hereby made of valuable services rendered in the preparation of the 1943 supplement by Wilbur E. Powers, B Sc., of the staff of the Board of Pharmacy of the State of New Jersey

H. V. A.
R. P. F.

April, 1943.

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The following articles did not appear in U.S.P. XI but are official in U.S.P. XII. However, some of them were previously official in N.F. VI, and a few of them appeared in supplements to U.S.P. XI.

ACIDUM AMINOACETICUM—Aminoacetic Acid

(Acid. Aminoacet.—Glycocoll, Glycine)

$C_2H_5O_2N$ Molecular weight, 75.07

$H_2N\ CH_2.COOH$

Aminoacetic Acid, when dried at 100° C. for 4 hours, contains not less than 18.4 per cent and not more than 18.8 per cent of N, corresponding to not less than 98.5 per cent of $C_2H_5O_2N$.

Storage.—Preserve in well-closed containers.

Summarized Description.

White, crystalline powder; odorless; sweetish taste; soluble in about 2 parts of water; very slightly soluble in alcohol and in ether.

For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 15.

Remarks.—This is the simplest of the amino acids and is used in the treatment of pseudohypertrophic and progressive muscular dystrophy, and myasthenia gravis. It should not be confused with the poisonous photographic developer "glycin." It has been synthesized by the action of ammonia on monochloracetic acid and may also be prepared by boiling gelatin or hippuric acid with hydrochloric acid.

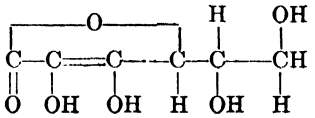
For further information, see Principles of Pharmacy, pp. 671, 674 (bibliography), 796, 948, 949, 951, 958 and 966.

Dose.—30 Gm. (8 drachms).

ACIDUM ASCORBICUM—Ascorbic Acid

(Acid. Ascorb.—Vitamin C)

$C_6H_8O_6$ Molecular weight, 176.12



Ascorbic Acid contains, when dried in a vacuum desiccator over sulfuric acid for 3 hours, not less than 99 per cent of $C_6H_8O_6$.

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White or slightly yellow crystals or powder; odorless; gradually darkens on exposure to light; in dry state reasonably stable in air but aqueous solution deteriorates in presence of air; soluble in about 3 parts of water and in about 30 parts of alcohol; insoluble in chloroform, in ether, and in benzene; melts 189°–192° C., specific rotation $[\alpha]^{25}_{D}$ in 10 per cent solution using 200-mm. tube is between +20.5 and +21.5.

For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 16.

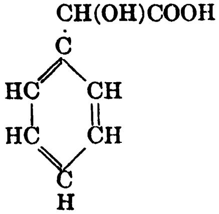
Remarks.—Also called cevitamic acid, antiscorbutic vitamin, cebione and redoxon. First isolated from lemons and then in 1832 from Hungarian paprika. Occurs in vegetables and fruits, especially in citrus fruits and the leafy parts of plants, but it is easily destroyed by heat and much is lost in cooking. Produced synthetically from sorbose or xylose. It is used in the prophylaxis and treatment of scurvy. It is also official in U.S.P. XII in the form of tablets. For further information, see pages 956 and 957, Principles of Pharmacy.

Dose.—50 mg. (¾ grain).

ACIDUM MANDELICUM—Mandelic Acid

(Acid. Mandel.—Racemic Mandelic Acid)

$C_8H_8O_3$ Molecular weight, 152.14



Mandelic Acid, when dried over sulfuric acid for 18 hours, contains not less than 99 per cent of $HC_8H_7O_3$.

Storage.—Preserve in well-closed, light-resistant containers.

Summarized Description.

White crystals or crystalline powder; odorless or has slight, aromatic odor; gradually darkens and decomposes on exposure to light; soluble in about 6.5 parts of water; freely soluble in alcohol and in ether; melts 118°–120° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 24–25.

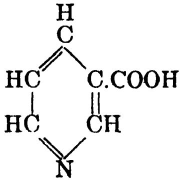
Remarks.—Also known as alpha-hydroxy-alpha-toluic acid, racemic or inactive mandelic acid, amygdalic, paramandelic, α-hydroxyphenylacetic, phenylglycollic or benzoylglycollic acid. It is made by the interaction of benzaldehyde, sodium bisulfite and sodium cyanide, and then by the subsequent hydrolysis of the resulting cyanhydrin. It is a nonmetabolizable substance, which when administered by mouth is excreted unchanged in the urine. If the *p*H of the urine is kept 5.5 or less it is rendered bactericidal or bacteriostatic against *Escherichia coli* and a number of other pathogenic organisms. To maintain proper *p*H of urine, it is often necessary to administer ammonium chloride.

Dose.—3 Gm. (45 grains).

ACIDUM NICOTINICUM—Nicotinic Acid

(Acid. Nicotin.—Niacin)

$C_6H_5O_2N$ Molecular weight, 123.11



Nicotinic Acid, when dried over sulfuric acid for 3 hours, contains not less than 99.5 per cent of $HC_6H_4O_2N$.

Storage.—Preserve in well-closed containers.

Summarized Description.

White crystals or crystalline powder; odorless or may have slight odor; soluble in 60 parts of water; freely soluble in boiling water and in boiling alcohol; soluble in aqueous solutions of alkali hydroxides and carbonates; almost insoluble in ether; melts 234°–237° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 25.

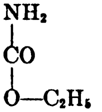
Remarks.—Also known as β or 3-pyridinecarboxylic acid. This is the factor obtained from Vitamin B by Elvehjem and was first prepared synthetically by Weide in 1873. It occurs in small quantities in rice and yeast. Nicotinic Acid is prepared by the oxidation of nicotine with nitric acid or potassium permanganate; it is also obtained by the oxidation of quinoline. It is a preventive and cure for pellagra. It is also official in U.S.P. XII in the form of tablets. For further information, see page 905 of Principles of Pharmacy.

Dose.—25 mg. (⅜ grain)

ÆTHYLIS CARBAMAS—Ethyl Carbamate

(Æthyl. Carbam.—Urethane)

$C_3H_7O_2N$ Molecular weight, 89.09



$$\begin{array}{l} NH_2 \\ | \\ CO \\ | \\ O—C_2H_5 \end{array}$$

Storage.—Preserve in well-closed containers, preferably at a temperature not above 30° C.

Summarized Description.

Colorless, columnar crystals or white granular powder; odorless or nearly so; cooling, saline taste; soluble in .5 part of water, in 1 part of alcohol, in 3 parts of glycerin, in about 1 part of chloroform, in about 2 parts of ether and in about 35 parts of olive oil.

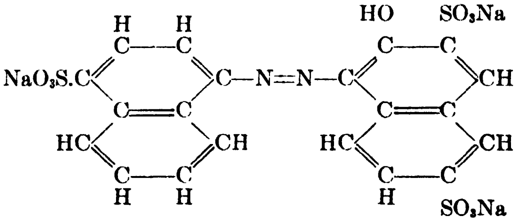
For *identification* and *tests for purity,* see U.S.P. XII, pp. 39 and 40.

Remarks.—Although this drug, which was previously official in N.F. VI, has been used as a hypnotic, antispasmodic, and sedative and is an antidote in poisoning by strychnine, resorcinol and picrotoxin, it has been introduced into U.S.P. XII as a pharmaceutic aid in preparing injection of quinine hydrochloride and ethyl carbamate, because it has the property of increasing the solubility of the quinine salt which results in a neutral solution. The injection is used in the treatment of varicose veins. Ethyl carbamate is prepared by heating urea with alcohol under pressure; by warming urea nitrate with alcohol and sodium nitrite. For further information, see page 755 of Principles of Pharmacy.

AMARANTHUM—Amaranth

(Amaranth.—F. D. and C. Red No. 2)

$C_{20}H_{11}N_2O_{10}S_3Na_3$ Molecular weight, 604.48



Amaranth is the trisodium salt of 1-(4-sulfo-1-naphthylazo)-2-naphthol-3,6-disulfonic acid.

Storage.—Preserve in well-closed containers.

Summarized Description.

Dark red brown powder soluble in about 15 parts of water; very slightly soluble in alcohol. 1 per cent aqueous solution is vivid red in color when viewed through a depth of 1 cm. and fairly stable towards light.

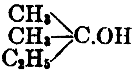
For further information, see pp 50–51 of U.S.P. XII.

Remarks.—Formerly official in N.F. VI. Also known as azo acid rubin 2B, fast red D and Bordeaux S. Permitted for use as a coloring agent in foods, drugs and cosmetics under Federal Food, Drug and Cosmetic Act. Also used in dyeing wool and silk as it is an exceptionally fast, light color. Solution of Amaranth (see page 24), formerly official in N.F. VI, is also now official in U.S.P. XII.

AMYLENI HYDRAS—Amylene Hydrate

(Amylen. Hydr.—Tertiary Amyl Alcohol)

$C_5H_{12}O$ Molecular weight, 88.15



$$\left.\begin{array}{l}CH_3\\CH_3\\C_2H_5\end{array}\right\rangle C.OH$$

Storage.—Preserve in tight containers.

Summarized Description.

Clear, colorless liquid; burning taste; camphoraceous odor; soluble in about 8 parts of water; miscible with alcohol, with chloroform, with ether and with glycerin; boils 97°–103° C.; specific gravity, 0.803–0.807.

For *identification* and *tests for purity,* see U.S.P. XII, p. 54.

Remarks.—Also known as dimethylethylcarbinol and tertiary pentanol. Introduced into the U.S.P. XII as a pharmaceutic necessity in the preparation of solution of tribromoethanol. Amylene Hydrate has hypnotic and sedative properties.

AQUA—Water

H_2O Molecular weight, 18.02

Water conforms to the requirements and tests summarized below.

Summarized Description.

Clear, colorless liquid; practically tasteless and odorless; meets the standards for freedom from *B. coli* required for potable water by the United States Public Health Service. For further *tests for purity,* see U.S.P. XII, p. 61.

Remarks.—Formerly official in N.F. VI and introduced for first time in first supplement of U.S.P. XI. Water is used in various menstrua for the extraction of drugs and in the preparation of distilled water, sterilized distilled water and Water for Injection. For further information, see Principles of Pharmacy, p. 413.

AQUA PRO INJECTIONE—Water for Injection

(Aq. pro Inject.)

Caution.—When "sterile water" or "sterile distilled water" for parenteral use is required or is dispensed as a vehicle, solvent, or diluent for substances to be administered parenterally, "Water for Injection" must be dispensed.

"Water for Injection" is water for parenteral use which has been distilled and sterilized within 24 hours. It is distilled, sterilized, and stored in sealed or other suitable sterile containers, so that it is free and remains free from pyrogens. Injection water conforms to the sterility test for liquids, U.S.P. XII, p. 609.

Sterilized "Water for Injection" preferably by Process C. See Sterilization Methods, U.S.P. XII, p. 616.

For further information as to use in *preparations, physical and chemical standards, pyrogen test* and *substances which may be added,* see U.S.P. XII, p. 66.

Remarks.—Water for Injection is intended for use in the preparation of aqueous solutions for parenteral use. See "Injections," p. 20.

BENTONITUM—Bentonite

(Bentonit.)

Bentonite is a native, colloidal, hydrated aluminum silicate.

Storage.—Preserve in well-closed containers.

Summarized Description.

Very fine powder or small granules, free from grit; odorless; tasteless; practically colorless; insoluble in water and organic solvents but in water swells to about eight times its volume forming an opalescent suspension or paste.

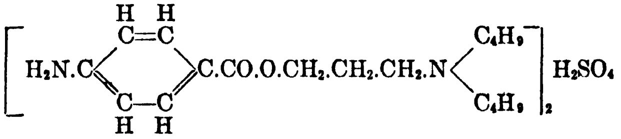
For *identification* and *tests for purity,* see U.S.P. XII, pp. 82–83.

Remarks.—Also known as wilkinite. It is a clay and is mined in the midwest of the U.S.A. and in Canada. Used as an emulsifier for oils and as a base for plasters. Used in Chalk Mixture U.S.P. XII for the first time as a suspending agent. A new product, Magma of Bentonite, has also been added to N.F. VII (see p. 52).
For further information, see Principles of Pharmacy, p. 549.

BUTACAINÆ SULFAS—Butacaine Sulfate

(Butacain. Sulf.)

$(C_{18}H_{80}N_2O_2)_2H_2SO_4$ Molecular weight, 710.95



Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

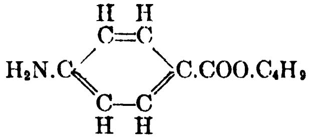
White, crystalline powder; odorless; affected by light; rapidly numbs the tongue when placed on it; slowly soluble in less than its own weight of water, dissolves more rapidly on heating; very soluble in warm alcohol and in acetone; slightly soluble in chloroform; insoluble in ether; melts 100°–103° C.
For *identification,* see pp. 89–90 of U.S.P. XII.

Remarks.—Also known as butyn sulfate. This drug is a local anesthetic proposed as a substitute for cocaine, particularly in surface anesthesia, as for the eye, nose and throat. It acts through intact mucosæ about as effectively as cocaine. For ophthalmologic work, usually used in 2 per cent solution. It is also used in rhinology and urogenital surgery; tooth extraction and other dental procedures.

BUTYLIS AMINOBENZOAS—Butyl Aminobenzoate

(Butyl. Aminobenz.—Normal Butyl Aminobenzoate)

$C_{11}H_{15}O_2N$ Molecular weight, 193.24



Storage.—Preserve in well-closed containers.

Summarized Description.

White, crystalline powder; odorless; tasteless; soluble in about 7000 parts of water, in dilute acids, in alcohol, in chloroform, in ether, and in fatty oils; slowly hydrolyzed when boiled with water; melts 57°–59° C.
For *identification* and tests for purity, see U.S.P. XII, pp. 90–91.

Remarks.—Also known as butesin. It is a local anesthetic and analgesic which is unsuitable for injection because of its slight solubility. It is used for ulcers, wounds and mucous surfaces either in pure form or diluted in the form of dusting powders, troches, ointments, suppositories, or oil solution. For further information, see p. 797 of Principles of Pharmacy.

CALCII MANDELAS—Calcium Mandelate

(Calc. Mandel.)

$Ca(C_8H_7O_3)_2$ Molecular weight, 342.35

Calcium Mandelate, when dried for 4 hours at 110° C., contains not less than 98.5 per cent of $(C_6H_5.CHOH.COO)_2Ca$.
Storage.—Preserve in well-closed containers.

Summarized Description.

White powder; odorless; slightly soluble in cold water; insoluble in alcohol; soluble in about 80 parts of boiling water.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 100–101.

Remarks.—Used in treating infections of the urinary tract as are other salts of mandelic acid. Bacteriostatic in the urine at a *p*H of 5.5 or less and to obtain this acidity it is sometimes necessary to give in conjunction with acid producing salts, such as ammonium chloride. Calcium Mandelate is used frequently by pediatricians in preference to the syrup of ammonium mandelate and other salts of mandelic acid. See also Mandelic Acid, p. 4.

Dose.—4 Gm. (60 grains).

CALCII PHOSPHAS TRIBASICUS—Tribasic Calcium Phosphate

(Calc. Phos. Tribas.—Precipitated Calcium Phosphate)

Tribasic Calcium Phosphate, after ignition to constant weight, contains an amount of phosphate (PO_4) corresponding to not less than 90 per cent of $Ca_3(PO_4)_2$ (310.20).

Summarized Description.

White powder; odorless; tasteless; permanent in air; almost insoluble in water; insoluble in alcohol; dissolves readily in diluted hydrochloric and nitric acids.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 101–103.

Remarks.—Also known as tertiary calcium phosphate. The technical product is called "bone ash." Formerly official in N.F. VI. It is used as an antacid and has an advantage over the alkaline hydroxides and alkali carbonates in that being less soluble, it tends to neutralize the excess acidity in the stomach but produces less systemic alkalinization. It is also a hemostatic and has been used in the treatment of bone diseases, caries, osteomyelitis, etc., because it has been shown that some of its calcium is absorbed. Also see Principles of Pharmacy, p. 528.

Dose.—1 Gm. (15 grains).

CALX SODICUM—Soda Lime

(Calx. Sod.)

Soda Lime for use in metabolism, anesthesia, and oxygen therapy contains calcium hydroxide and sodium or potassium hydroxide or both in granular form.

Soda Lime is available in two forms, *Low-Moisture* Soda Lime which contains less than 9 per cent of moisture and *High-Moisture* Soda Lime which contains not less than 9 per cent and not more than 19 per cent of moisture.

Soda Lime may contain an indicator which is inert with respect to its reactivity with ether, nitrous oxide, ethylene, and cyclopropane and which changes color when the absorption capacity of the Soda Lime for carbon dioxide is exhausted. When present, the nature and color change of the indicator must be stated on the label of the container.

Storage.—Preserve in tight containers. This is a change from U.S.P. XII authorized after publication.

Summarized Description.

White or grayish white but may have a color if an indicator has been added; granules pass completely through a No. 2 standard mesh sieve, and not more than 2 per cent passes through a No. 40 standard mesh sieve; mesh of Soda Lime should be indicated on label and not more than 10 per cent passes through the finer mesh indicated on the label.

For *identification* and *further tests,* see U.S.P. XII, pp. 103–104, and Sheet Supplements to U.S.P. XII.

Remarks.—Used to absorb CO_2 in basal metabolism tests, in rebreathing anesthesia machines, in submarines and in carbon determinations.

CAPSULÆ—Capsules

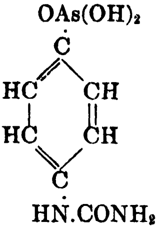
For the first time capsules as a form of medication appear in U.S.P. XII. There are twelve monographs for capsules and a table listing these appears on page 9. For *identification, assay, storage, dose* and other information, see U.S.P. XII, pp. 105–113. For general information see Principles of Pharmacy, pp. 320–327.

Official Latin Title	*Official English Title and Synonym, if Any*	*Prescribed Limits of Labeled Amount of Active Ingredients Including All Tolerances*
Capsulæ Ammonii Chloridi	Ammonium Chloride Capsules	95 to 105 per cent
Capsulæ Carbonei Tetrachloridi	Carbon Tetrachloride Capsules	92 to 108 per cent
Capsulæ Digitalis	Digitalis Capsules	95 to 105 per cent
Capsulæ Diphenylhydantoini Sodici	Diphenylhydantoin Sodium Capsules	93 to 107 per cent
Capsulæ Ferri et Ammonii Citratum	Iron and Ammonium Citrates Capsules	Contain an amount of iron (Fe) corresponding to 15.5–19.5 per cent of labeled amount of iron and ammonium citrates.
Capsulæ Olei Chenopodii	Oil of Chenopodium Capsules. *Syn.*—Oil of American Wormseed Capsules	95 to 105 per cent. Oil from capsules contains not less than 65 per cent of ascaridol, $C_{10}H_{16}O_2$.
Capsulæ Olei Hippoglossi	Halibut Liver Oil Capsules	95 to 105 per cent. Oil from capsules contains in each Gm. not less than 60,000 U.S.P. Units of Vitamin A. Capsules shall be labeled to contain either 5000 or 25,000 U.S P. Units of Vitamin A per capsule.
Capsulæ Oleovitaminæ A	Oleovitamin A Capsules	95 to 105 per cent. Oil conforms to definition for Oleovitamin A, U.S.P. XII, p. 310, but may be adjusted in Vitamin A potency. Capsules shall be labeled to contain either 5000 or 25,000 U.S.P. units of Vitamin A per capsule.
Capsulæ Oleovitaminæ A et D Concentratæ	Concentrated Oleovitamin A and D Capsules. *Syn.*—Concentrated Vitamin A and D Capsules	95 to 105 per cent. Oil conforms to definition for Oleovitaminæ A et D Concentrata, U.S.P. XII, p. 312, but may be adjusted in Vitamin A and Vitamin D potency. Capsules shall be labeled to contain 5000 U.S.P. Units of Vitamin A and 1000 U.S.P. Units of Vitamin D per capsule.
Capsulæ Pentobarbitali Sodici	Pentobarbital Sodium Capsules. *Syn.*—Soluble Pentobarbital Capsules	90 to 105 per cent
Capsulæ Tetrachloroæthyleni	Tetrachloroethylene Capsules	94 to 106 per cent
Capsulæ Theobrominæ et Sodii Acetatis	Theobromine and Sodium Acetate Capsules	Contain an amount of theobromine, $C_7H_8N_4O_2$, equivalent to 53–67 per cent of the labeled amount of theobromine and sodium acetate.

CARBARSONUM—Carbarsone

(Carbarson.)

$C_7H_9AsN_2O_4$ Molecular weight, 260.07



Carbarsone, when dried at 80° C. for 6 hours, contains not less than 28.1 per cent and not more than 28.8 per cent of arsenic (As).

Storage.—Preserve in well-closed containers.

Summarized Description.

White powder, almost odorless and having a slightly acid taste; slightly soluble in water and in alcohol; nearly insoluble in chloroform and in ether; soluble in solutions of alkali hydroxides and carbonates; melts 169°–172° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 114.

Remarks.—Also called arsanilic acid. Used in treatment of intestinal amebiasis and is usually administered by mouth; in acute amebic dysentery, retention enemas may be employed; also has been used in the treatment of Trichomonas vaginitis.

Dose.—0.2 Gm. (3 grains).

CARBASUS ABSORBENS—Absorbent Gauze

(Carbas. Absorb.—Gauze, Plain Gauze, Nonsterilized Absorbent Gauze)

Absorbent Gauze consists of well bleached cotton cloth of plain weave.

Storage.—Preserve in a well-closed container. The type, thread count, length, and width of the Gauze must be stated on the container, and the designation "unsterilized" or "not sterilized" must appear prominently thereon.

Summarized Description.

White cotton cloth of various thread counts and weights, of which there are seven commercial types varying from one another in warp, filling and weight.

For table of commercial designations in type and in terms of *thread count* and the *standard weight* in grams per linear yard, and for *identification* and other *tests,* see U.S.P. XII, pp. 114–116.

CARBASUS ABSORBENS ADHÆSIVUS—Adhesive Absorbent Gauze

(Carbas. Absorb. Adhæs.—Adhesive Absorbent Compress)

Storage.—Adhesive Absorbent Gauze must be packaged individually in such manner that the sterility is maintained until the individual package is opened for use, and the individual packages must be grouped in a second protective container. Adhesive Absorbent Gauze shall be sterilized in the individual packages. The container shall bear a statement to the effect that the sterility of the gauze cannot be guaranteed if the individual package bears evidence of damage or has been previously opened. Preserve preferably at a temperature which does not exceed 30° C. and do not expose to sunlight.

Summarized Description.

An individual dressing prepared by affixing a plain absorbent compress to a strip of adhesive plaster; adhesive surface protected; gauze must be sterile and be protected from contamination by suitable packaging.

For details of *absorbent compress* and further description, see U.S.P. XII, p. 116.

CARBASUS ABSORBENS STERILIS—Sterile Absorbent Gauze

(Carbas. Absorb. Steril.—Sterile Gauze)

Sterile Absorbent Gauze is absorbent gauze which has been rendered sterile and protected from contamination. Sterile Absorbent Gauze may be supplied in various lengths and widths, and in the form of rolls or folds.

Storage.—Each unit shall be so packaged individually that the sterility of the unit is maintained until the package is opened for use. Sterile Absorbent Gauze shall be sterilized in the package, and the package shall bear a statement to the effect that the sterility of the gauze cannot be guaranteed if the package bears evidence of damage or has been previously opened. The length, width, and type of the gauze shall be stated upon the package.

Summarized Description.

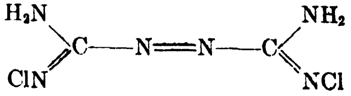
Complies with the definition, description, and tests under Carbasus Absorbens, U.S.P. XII, p. 114.

For further information, see U.S.P. XII, p. 117.

CHLOROAZODINUM—Chloroazodin

(Chloroazodin.)

$C_2H_4Cl_2N_6$ Molecular weight, 183.01



Chloroazodin contains the equivalent of not less than 37.5 per cent and not more than 39.5 per cent of active chlorine (Cl).

Storage.—Preserve in a well-closed, light-resistant containers, preferably in a cold place.

Summarized Description.

Bright yellow needles or flakes; faint odor suggestive of chlorine; slightly burning taste; solutions in glycerin and in alcohol decompose rapidly on warming; all solutions of this drug decompose on exposure to light and the drug itself decomposes explosively at 155° C. Contact with metals accelerates this decomposition. Very slightly soluble in water, sparingly soluble in alcohol, slightly soluble in glycerin and triacetin, and very slightly soluble in chloroform.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 128–129.

Remarks.—This is a germicide also known as azochloramid which is similar in action to chloramine-T, dichloramine-T, and diluted solution of sodium hypochlorite, over which it is claimed to have an advantage in that it possesses lower reactivity with extraneous organic matter and higher bactericidal activity in the presence of organic matter. Solutions of this germicide are used for dressing, packing, or irrigating infected wounds and cavities. It is highly active against both gram-positive and negative organisms. A solution of this drug in glyceryl triacetate is also official in U.S.P. XII.

CHORDA CHIRURGICALIS—Surgical Gut

(Chord. Chirurg.—Surgical "Catgut," "Catgut" Suture)

Surgical Gut consists of sterile gut prepared from the longitudinally split segment of submucous connective tissue of the small intestine of healthy sheep, *Ovis aries* Linné (Fam. *Bovidæ*).

Storage.—Preserve each strand in an individual, hermetically sealed glass tube.

Description.—Surgical Gut is either plain gut which has not been treated in any manner which will alter its normal rate of digestibility, known as *Type A, Plain or Untreated,* or it is gut which has been tanned or otherwise treated so that it will resist digestion for longer but varying periods of time, and known respectively as *Type B, Mild Treatment; Type C, Medium Treatment;* and *Type D, Prolonged*

Treatment. One form of treatment is frequently referred to as *Chromic.* The foregoing types mentioned are supplied as *Boilable* or as *Non-boilable* Surgical Gut. Surgical Gut is uniformly and firmly twisted.

Caution—The tubes of Surgical Gut marked "Non-boilable" must not be subjected to heat. Tubes marked "Boilable" may be heated for purposes of sterilizing the outside of the tube.

For *tests, standards* and *labeling,* see U.S.P. XII, pp. 131–133.

Remarks.—This important aid in surgical practice became official in Supplement II of U.S.P. XI.

CHORDA SERICA CHIRURGICALIS—Surgical Silk

(Chord. Ser. Chirurg.—Silk Sutures)

Surgical Silk consists of the thread prepared from the cocoon filaments of glutinous gum which are secreted or spun by the mulberry silkworm, *Bombyx mori* Linné (Fam. *Bombycidæ*). The strands may be processed to form threads of various diameters by braiding or twisting, or a combination of both.

Note.—Surgical Silk may be sterilized by exposing the strands to saturated steam at 15 pounds pressure (121.5° C.) for 30 minutes.

Storage.—Preserve in well-closed containers.

Description.—Surgical Silk may be white or colored. *White* Surgical Silk consists of degummed silk which has not been subjected to any bleaching process. *Colored* Surgical Silk consists of degummed silk which has been "iron dyed" or dyed with a harmless vegetable dye, or a certified coal tar color. All uncombined dye shall be removed from the material, so that the color of the suture will not bleed into the tissue.

Surgical Silk may consist of pure silk which is capillary, known as Type A, *Untreated* or *Capillary;* or it may consist of pure silk which has been treated to reduce its capillarity, known as Type B, *Treated* or *Non-capillary.*

For *tests, standards* and *labeling,* see U.S.P. XII, pp. 133–134.

CHORDA SERICA CHIRURGICALIS STERILIS—Sterile Surgical Silk

(Chord. Ser. Chirurg. Steril.—Sterile Silk Sutures)

Sterile Surgical Silk is Surgical Silk which has been rendered sterile and protected from contamination by suitable packaging.

Storage.—Preserve in hermetically sealed glass tubes or in other containers holding not more than 2 strands; must be sterilized in container. For details of storage, see U.S.P. XII.

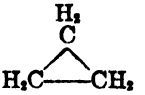
Sterile Surgical Silk agrees with the description and conforms to the requirements for *length* and *diameter,* under Chorda Serica Chirurgicalis, U.S.P. XII, p. 133.

For further information, see U.S.P. XII, p. 134.

CYCLOPROPANUM—Cyclopropane

(Cycloprop.—Trimethylene)

C_3H_6 Molecular weight, 42.08



Cyclopropane contains not less than 99 per cent by volume of C_3H_6.

The label must bear the following statement: *"Caution—Cyclopropane is inflammable and its mixture with oxygen or air may explode when brought in contact with a flame or other causes of ignition."*

Storage.—Preserve in tight containers.

Summarized Description.

Colorless gas; characteristic odor similar to petroleum benzin; pungent taste; 1 liter weighs 1.879 Gm. (S.T.P.); soluble in about 2.7 parts of water at 15° C.; freely soluble in alcohol; soluble in fixed oils.

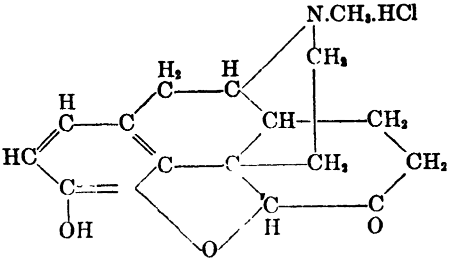
For *tests for purity* and *assay,* see U.S.P. XII, pp. 147–148.

Remarks.—Used as inhalation anesthetic with oxygen in ratios varying from 15 per cent cyclopropane and 85 per cent oxygen to rarely 40 per cent cyclopropane and 60 per cent oxygen. One of the advantages of this gas is that it is effective in concentrations furnishing an adequate supply of oxygen.

DIHYDROMORPHINONI HYDROCHLORIDUM—Dihydromorphinone Hydrochloride

(Dihydromorph. Hydrochlor.)

$C_{17}H_{19}O_3N.HCl$ Molecular weight, 321.80



Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

Fine, white, crystalline powder; odorless; affected by light; soluble in about 3 parts of water; sparingly soluble in alcohol, and nearly insoluble in ether.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 152–153.

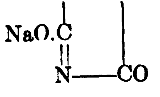
Remarks.—Also known as dilaudid hydrochloride. Obtained by reducing morphine with hydrogen in HCl solution in the presence of a catalyst. Dilaudid itself is very similar to morphine in both its pharmacological and chemical properties. It is more toxic than morphine but its effective dose is much smaller. It has morphine's action on the respiratory system and relieves pain but is claimed to be less nauseating. This drug comes within the scope of the federal narcotic regulations. The principal use is as a narcotic and sedative and it is usually marketed as oral or hypodermic tablets and as rectal suppositories. The tablets are official in U.S.P. XII.

Dose.—2 mg. ($\frac{1}{30}$ grain).

DIPHENYLHYDANTOINUM SODICUM—Diphenylhydantoin Sodium

(Diphenylhydant. Sod.)

$C_{15}H_{11}N_2O_2Na$ Molecular weight, 274.25



Diphenylhydantoin Sodium, when dried for 4 hours at 100° C., contains not less than 90.5 per cent and not more than 92 per cent of diphenylhydantoin ($C_{15}H_{12}N_2O_2$).

Storage.—Preserve in tight containers.

Summarized Description.

White powder; odorless; somewhat hygroscopic; on exposure to air gradually absorbs CO_2 with liberation of diphenylhydantoin; freely soluble in water forming usually a somewhat turbid solution due to partial hydrolysis; soluble in alcohol; practically insoluble in ether and chloroform.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 153–154.

Remarks.—Also known as phenytoin sodium. It is an anticonvulsant with a relatively weak hypnotic action. Used in the treatment of epileptic patients who are not benefited by phenobarbital or bromides and those in whom these drugs induce disagreeable side actions. It is also official in U.S.P. XII in the form of capsules.

Dose.—0.1 Gm. (1½ grains).

ELIXIR PHENOBARBITALI—Elixir of Phenobarbital

(Elix. Phenobarb.)

Elixir of Phenobarbital contains, in each 100 cc., not less than 0 37 Gm. and not more than 0.43 Gm. of Phenobarbital.

Alcohol Content.—17 to 20 per cent by volume.

Storage.—Preserve in tight, light-resistant containers.

Condensed Recipe.

Ingredients.—Phenobarbital, 4 Gm.; tincture of sweet orange peel, 30 cc.; solution of amaranth (U.S.P. XII), 10 cc.; alcohol, 175 cc.; glycerin, 100 cc.; sucrose, 400 Gm.; distilled water enough to make 1000 cc.

Manipulation.—The phenobarbital is dissolved in the alcohol, and the tincture of sweet orange peel, the glycerin, the solution of amaranth, and enough distilled water to make 700 cc. are added in the order named. The sugar is dissolved in this solution by agitation. Water is added to make 1000 cc. and the elixir is filtered if necessary.

For *assay,* see U.S.P. XII, p. 155. Note, however, that this is not the formula appearing in U.S.P. XII. The formula above has been adopted for the period of the war or until the order is rescinded by official action.

Remarks.—This elixir was introduced to meet the need for a liquid barbiturate and is especially useful as a form of medication for children. Phenobarbital is used as a sedative and hypnotic and also as an antispasmodic in epilepsy. For further information see Principles of Pharmacy, p. 757.

Dose.—4 cc. (1 fluidrachm). This dose contains 16 mg. (¼ grain) of phenobarbital.

EMPLASTRUM ADHÆSIVUM STERILE—Sterile Adhesive Plaster

(Emp. Adhæs. Steril.—Sterile Adhesive Tape)

Storage.—Each unit packaged individually and sterilized in package; preserve preferably at a temperature not above 30° C. and do not expose to sunlight. For required statement on package, see U.S.P. XII, pp. 157–158.

Summarized Description.

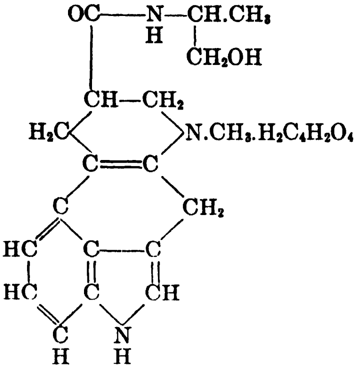
Consists of a mixture, having pressure-sensitive properties, spread evenly upon fabric with the adhesive surface protected; suitably packaged to protect from contamination and must be sterilized in package.

For further details, see U.S.P. XII, pp. 157–158.

ERGONOVINÆ MALEAS—Ergonovine Maleate

(Ergonov. Mal.)

$C_{19}H_{23}N_3O_2.C_4H_4O_4$ Molecular weight, 441.47



The maleate of an alkaloid obtained from ergot. Ergonovine Maleate, when dried to constant weight over sulfuric acid, contains not less than 98 per cent of $C_{19}H_{23}N_3O_2.C_4H_4O_4$.

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White, or faintly yellow, microcrystalline powder; odorless; affected by light; soluble in about 36 parts of water, and in about 120 parts of alcohol; insoluble in ether and in chloroform; melts with decomposition at about 167° C.; specific rotation $[\alpha]^{25}_{D}$ of a 1 per cent aqueous solution is not less than +48° and not more than +57° when determined in a 100-mm. tube.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 165 and 166.

Remarks.—The alkaloid ergonovine is also known as ergometrine, ergobasine, ergostetrine, ergotocine, and ergotrate. The alkaloid is considered to be the most important active constituent of ergot. Given orally it acts promptly to bring on vigorous uterine contractions. This drug is also official in U.S.P. XII in the form of tablets.

Dose.—0.5 mg. (1/120 grain).

ERGOTAMINÆ TARTRAS—Ergotamine Tartrate

(Ergotam. Tart.)

$(C_{33}H_{35}N_5O_5)_2.H_2C_4H_4O_6$ Molecular weight, 1312.67

The tartrate of an alkaloid obtained from ergot.

Storage.—Preserve in well-closed containers protected from light and heat.

Summarized Description.

Colorless crystals or white, crystalline powder, usually containing solvent of crystallization which is lost in a high vacuum; soluble in about 500 parts of water and in 500 parts of alcohol; darkens on heating at 177° C. and decomposes at 184° C.; specific rotation $[\alpha]^{25}_{D}$ of a 0.4 per cent solution in chloroform using a 100-mm. tube is not less than −125° and not more than −155°.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 167–168.

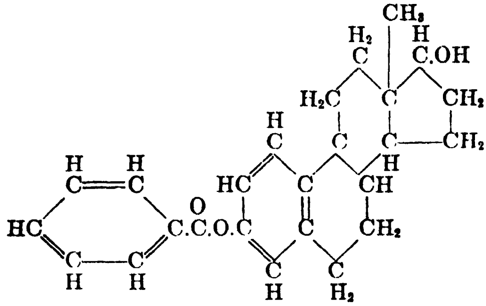
Remarks.—Also known as gynergen. It is used as a uterine contractor where ergot is indicated, in postpartum and postabortal hemorrhage, after curettage and in the treatment of migraine. It also has been used in conditions in which there is believed to be overactivity of the sympathetic nervous system. There is danger of poisoning from long continued use or overdosage. The tablets are also official in U.S.P. XII.

Dose.—0.5 mg. (1/120 grain).

ESTRADIOLIS BENZOAS—Estradiol Benzoate

(Estradiol. Benz.—Œstradiol Benzoate)

$C_{25}H_{28}O_3$ Molecular weight, 376.47



The benzoate of alpha-estradiol.

Storage.—Preserve in well-closed, light-resistant containers.

Summarized Description.

White or slightly yellow to brownish, crystalline powder; odorless; stable in air; almost insoluble in water; soluble in alcohol, in acetone, and in dioxane; slightly soluble in ether, and sparingly soluble in sesame and other vegetable oils; melts 191°–196° C.; specific rotation [α] of a 2 per cent solution in dioxane using a 100-mm. tube is not less than +58° and not more than +63°.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 169–170.

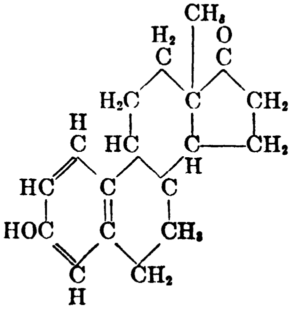
Remarks.—Also known as progynon B and dihydromenformone. Used in functional amenorrhea, scanty menstruation, menopausal disturbances, delayed puberty, sexual frigidity and functional sterility.

Dose.—Oral, 1 mg. (1/60 grain).

ESTRONUM—Estrone

(Estron.—Theelin, Œstrone)

$C_{18}H_{22}O_2$ Molecular weight, 270.36



Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

Small, white crystals or white, crystalline powder; odorless; stable in air; slightly soluble in water; soluble in alcohol, in acetone, in dioxane, and in solutions of fixed alkali hydroxides; melts 258°–262° C.; optical rotation [α] in a 1 per cent solution in dioxane using a 200-mm. tube is not less than +155° and not more than +165°.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 170–171.

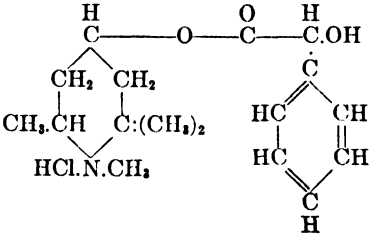
Remarks.—Also known as destrone, folliculin, œstroform, menoformon, and ketohydroxyestrin. It is a female sex hormone first isolated in crystalline form from the urine of pregnant women by Doisy, Veler and Thayer in 1929. The estrogenic activity of 0.1 microgram (1 ten millionth of a gram) of a standard preparation of estrone constitutes one international unit. Used in treatment of symptoms of menopause, natural or artificial; of symptoms of gonorrheal vaginitis of children in which case it is usually given in glycerogelatin suppositories; and in scanty menstruation.

Dose.—Intramuscular, 1 mg. (1/60 grain).

EUCATROPINÆ HYDROCHLORIDUM—Eucatropine Hydrochloride

(Eucatrop. Hydrochlor.)

$C_{17}H_{25}O_3N.HCl$ Molecular weight, 327.84



Eucatropine Hydrochloride, when dried over sulfuric acid for 4 hours, contains not less than 86 per cent and not more than 89 per cent of eucatropine ($C_{17}H_{25}O_3N$).

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White, granular powder; odorless; very soluble in water; freely soluble in alcohol and in chloroform; insoluble in ether; melting point not below 183° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 173.

Remarks.—Also known as euphthalmine hydrochloride. Used as an aid in ophthalmoscopic examination in place of atropine, homatropine and other mydriatics. Produces mydriasis of brief duration quickly and free from anesthetic action, pain, corneal irritation or increase in intra-ocular tension; has little or no effect on accommodation. Very similar to atropine in its general effect but differs in that it does not produce paralysis of accommodation.

EXTRACTUM PERPOLITIONUM ORYZÆ—Extract of Rice Polishings

(Ext. Perpol. Oryz.—Extract of Tikitiki, Extract of Rice Bran, Extracto de Salvado)

Extract of Rice Polishings contains, in each cc., not less than 20 U.S.P. Units of Vitamin B_1, and represents approximately 14.5 Gm. of Rice Polishings.

Storage.—Preserve in tight containers.

Summarized Preparation and Description.

Prepared by macerating rice polishings with a mixture of 3 volumes of alcohol and 1 volume of distilled water for 48 hours and then concentrating the supernatant and expressed liquid after filtering with heat under vacuum. The residue is mixed with alcohol, allowed to stand and the supernatant liquid is decanted, filtered and evaporated at a low heat under vacuum to an extract and then sealed in containers. Not more than 0.2 per cent of benzoic acid may be added as a preservative.

It is a dark brown, viscous liquid; odor of burnt sugar; sweetish taste; miscible with cold water; more readily miscible with warm water; specific gravity 1.28–1.32 at 27.5° C.

For *identification* and *assay* for Vitamin B_1, see U.S.P. XII, pp. 181–182.

Remarks.—This is an economical source of Vitamin B_1 and was given pharmacopoeial recognition at the request of the government of the Philippine Islands. For uses of Vitamin B_1, see Thiamine Hydrochloride, p. 45.
Dose.—8 cc. (2 fluidrachms).

FERRI SULFAS EXSICCATUS—Exsiccated Ferrous Sulfate

(Ferr. Sulf. Exsic.—Dried Ferrous Sulfate)

Exsiccated Ferrous Sulfate contains not less than 80 per cent of anhydrous ferrous sulfate ($FeSO_4$).
Storage.—Preserve in well-closed containers.

Summarized Description.
Grayish white powder which dissolves slowly in water and is insoluble in alcohol.
For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 186.

Remarks.—Was official in U.S.P. X but not in U.S.P. XI. This dried form is much easier to capsulate than the crystals and is also more convenient in the manufacture of pills and tablets. It is a hematinic and astringent and is taken internally in anemia to increase hemoglobin of blood and is used externally in leukorrhea because of its astringent action. It is used extensively in veterinary medicine. Ferrous Sulfate Tablets are official in U.S.P. XII. For further information, see Principles of Pharmacy, pp. 176 and 565.
Dose.—0.2 Gm. (3 grains).

GELATUM ALUMINI HYDROXIDI—Aluminum Hydroxide Gel

(Gel. Alum. Hydrox.—Colloidal Aluminum Hydroxide)

Aluminum Hydroxide Gel is an aqueous suspension containing the equivalent of not less than 3.6 per cent and not more than 4.4 per cent of Al_2O_3, chiefly in the form of the hydrous oxide of aluminum.
Note.—Sufficient oil of peppermint, glycerin, sucrose, or saccharin may be added for flavoring and other purposes. Sodium benzoate in an amount not exceeding 0.5 per cent may be added as a preservative.
Storage.—Preserve in well-closed containers and avoid freezing.

Summarized Description.
White, viscous suspension, translucent in thin layers. Small amounts of water may separate on standing.
For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 198–199.

Remarks.—It is a mild astringent and desiccant and is prescribed as an antacid and adsorbent. It acts also as a protective for inflamed or ulcerated areas of the gastrointestinal tract and is used in cases of peptic ulcer to promote healing, relieve pain and contract hemorrhage. It is also taken in cases of gastric hyperacidity, diarrhea and cholera. For general information, see Principles of Pharmacy, p. 548.
Dose.—8 cc. (2 fluidrachms).

GELATUM ALUMINI HYDROXIDI SICCUM—Dried Aluminum Hydroxide Gel

(Gel. Alum. Hydrox. Sic.)

Dried Aluminum Hydroxide Gel, when ignited to constant weight, yields not less than 50 per cent of Al_2O_3.
Storage.—Preserve in tight containers.

Summarized Description.
White, amorphous powder; tasteless; odorless; insoluble in water and in alcohol; soluble in diluted mineral acids and in solutions of fixed alkalies.
For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 199–200.

Remarks.—Administered suspended in milk or in tablet form as an antacid and as a protective in peptic ulcer. Also used as a dusting powder for inflammation of the skin; as a siccative for foul and gangrenous wounds; and in weeping dermatosis. Often prescribed in an ointment base. Base for Gelatum Alumini Hydroxidi, U.S.P. XII.

Dose.—0.6 Gm. (10 grains).

GLOBULINUM IMMUNE HUMANUM—Human Immune Globulin

(Glob. Immun. Human.—Measles Prophylactic, Placental Extract**)**

Human Immune Globulin is a sterile solution of antibodies obtained from the placentae expelled by healthy women (*Homo sapiens*). Each preparation shall be composed of a pool from at least ten individuals. Human Immune Globulin complies with the requirements of the National Institute of Health of the United States Public Health Service.

Storage.—Preserve at a temperature between 2° and 10° C., preferably at lower limit; must be dispensed in the manufacturer's original unopened glass container.

Summarized Description.

Transparent or slightly opalescent liquid; faint brownish, yellowish, or greenish color; nearly odorless or has odor due to preservative; may have slight, granular deposit.

For further information and *regulations,* see U.S.P. XII, p. 201.

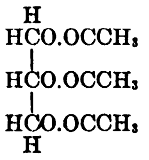
Remarks.—This preparation is used both for the modification and prevention of measles. The former is preferred as it confers active immunity for a long period of time whereas if injected for prevention, the passive immunity acquired is only of short duration. Globulin is prepared by extracting placental tissue expelled by healthy human mothers with sodium chloride solution and then treating the extract in such a manner as to concentrate the active substances and reduce the nonactive constituents.

Dose.—Intramuscular, for modification, 2 to 5 cc. (30–75 minims); for prevention, 2 to 10 cc. (30–150 minims).

GLYCERYLIS TRIACETAS—Glyceryl Triacetate

(Glyceryl. Triacet.—Triacetin)

$C_9H_{14}O_6$ Molecular weight, 218.20



$$\begin{array}{c}\text{H}\\ \text{HCO.OCCH}_3\\ |\\ \text{HCO.OCCH}_3\\ |\\ \text{HCO.OCCH}_3\\ \text{H}\end{array}$$

Storage.—Preserve in tight containers with no contact with metals.

Summarized Description.

Colorless liquid; somewhat oily; slight, fatty odor; bitter taste; soluble in water; miscible with alcohol, with ether, and with chloroform; insoluble in carbon disulfide; specific gravity 1.154–1.158; not less than 95 per cent distils between 257° and 260° C.; refractive index 1.4288–1.4296.

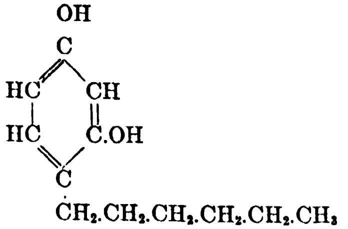
For *identification* and *tests for purity,* see U.S.P. XII, pp. 205–206.

Remarks.—This is a solvent for chloroazodin and the resulting solution may be used on wounds directly or diluted with olive oil. See remarks under chloroazodin, p. 11. A solution of chloroazodin in triacetin is also official in U.S.P. XII.

HEXYLRESORCINOL—Hexylresorcinol

(Hexylresorcin.)

$C_{12}H_{18}O_2$ Molecular weight, 194.26



Hexylresorcinol, when dried to constant weight over sulfuric acid, contains not less than 98 per cent of $C_{12}H_{18}O_2$.

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White, needle-shaped crystals; faint, fatty odor; sharp, astringent taste; produces a sensation of numbness when placed on tongue; acquires a brownish pink tint on exposure to light and air; soluble in about 2000 parts of water; freely soluble in alcohol, in glycerin, in ether, in chloroform, in benzene, and in vegetable oils; melts at a temperature not below 62° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 208–209.

Remarks.—Also known as caprokol and crystoids anthelmintic. This is an antiseptic and germicide which is given in urinary and other infections. It is also used in the eradication of some intestinal parasites such as hookworms, pinworms and ascaris. Has been used as a general disinfectant, dressing for wounds in strengths up to 1 in 1000 and in weaker strengths as an antiseptic gargle. Usually administered in solution in olive oil as contact with oral tissues must be avoided. Also see Principles of Pharmacy, p. 777.

Dose.—Anthelmintic, 1 Gm. (15 grains).

INJECTIONES—Injections

Injections have been introduced into U.S.P. XII for the first time and are solutions and suspensions of drugs indicated for parenteral administration. Some of them were official in N.F. VI under the term "Ampuls." The terms "parenteral" and "for injection" as used in U.S.P. XII refer to the administration of a drug under one or more layers of the skin or mucous membranes.

All aqueous vehicles, diluents, and solvents used in the preparation of Injections must be pyrogen-free. It is permissible to use in place of Water for Injection when so designated in the individual monographs for Injections, sterile isotonic solution of sodium chloride, sterile isotonic solution of three chlorides, or another suitable aqueous solvent or vehicle.

It is preferable to prepare, package, seal and sterilize the completed unit of an Injection in one working day but if this is impracticable the U.S.P. gives directions for storage. Preservatives, other substances, and bacteriostatic agents may be added in certain cases as provided for under the monograph for Injections in the U.S.P. XII, pp. 219–222. Here also may be found the regulations with respect to packaging of Injections in single or multiple doses, the method for the determination of the volume of Injection in containers, required labeling, and additional information on the preparation of Injections.

For further information, see U.S.P. XII, pp. 222–249, and Principles of Pharmacy, pp. 988–993.

There are twenty-five monographs in U.S.P. XII on Injections. Of this number four; namely, Injectio Hepatis, Injectio Histaminæ Phosphatis, Injectio Parathyroidei, and Injectio Pituitarii Posterioris, appeared in U.S.P. XI as Liquors. Injectio Insulini was first introduced into the Second Supplement of U.S.P. XI. Following is a table of these Injections and for completeness all twenty-five are included. For *identification, tests for purity, assay, sizes, dose* and other information, see U.S.P. XII, pp. 222–250. Information on the four Injections mentioned above which were official in U.S.P. XI as Liquors can also be found in Principles of Pharmacy.

Official Latin Title, English Title and Synonym, if Any	*Brief Description*	*Prescribed Limits of Labeled Amount of Active Ingredients Including All Tolerances*
Injectio Bismuthi et Potassii Tartratis: Bismuth and Potassium Tartrate Injection (Bismuth and Potassium Tartrate Ampuls)	Sterile solution in water for injection or sterile suspension in a suitable fixed oil.	Contains an amount of bismuth (Bi) equivalent to 57–66 per cent of labeled amount of bismuth and potassium tartrate.
Injectio Bismuthi Subsalicylatis: Bismuth Subsalicylate Injection (Bismuth Subsalicylate Ampuls)	Sterile suspension in a suitable fixed oil.	Contains an amount of bismuth (Bi) equivalent to 53–62 per cent of labeled amount of bismuth subsalicylate.
Injectio Caffeinæ et Sodii Benzoatis: Caffeine and Sodium Benzoate Injection (Caffeine and Sodium Benzoate Ampuls)	Sterile solution in water for injection.	Contains an amount of anhydrous caffeine equivalent to 45–52 per cent, and an amount of sodium benzoate equivalent to 47.5–55.5 per cent of labeled amount of caffeine and sodium benzoate.
Injectio Calcii Gluconatis: Calcium Gluconate Injection (Calcium Gluconate Ampuls)	Sterile solution in water for injection.	95–105 per cent.
Injectio Dextrosi: Dextrose Injection (Dextrose Ampuls)	Sterile solution in water for injection.	95–105 per cent.
Injectio Dextrosi et Sodii Chloridi: Dextrose and Sodium Chloride Injection (Dextrose and Sodium Chloride Ampuls)	Sterile solution in water for injection.	95–105 per cent of labeled amount of dextrose and of sodium chloride.
Injectio Digitalis: Digitalis Injection (Digitalis Ampuls)	Sterile solution of one or more of the glycosides or therapeutically desirable and cardioactive constituents of digitalis in water for injection.	Potency to be indicated on label in terms of U.S.P. Digitalis Units.
Injectio Emetinæ Hydrochloridi: Emetine Hydrochloride Injection (Emetine Hydrochloride Ampuls)	Sterile solution in water for injection.	Contains an amount of anhydrous emetine hydrochloride ($C_{29}H_{40}N_2O_4.2HCl$) equivalent to 84–94 per cent of labeled amount of emetine hydrochloride.
Injectio Epinephrinæ Hydrochloridi: Epinephrine Hydrochloride Injection (Epinephrine Hydrochloride Ampuls)	Sterile solution in water for injection.	Potency shall be stated on label in terms of quantity of U.S.P. Epinephrine Reference Standard to which it is equivalent.
Injectio Hepatis: Liver Injection (Liquor Hepatis Purificatus U.S.P. XI, Liver Extract for Parenteral Use)	Sterile solution in water for injection of that soluble thermostable fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons suffering from pernicious anemia.	The approximate anti-anemia potency of Liver Injection upon parenteral administration in pernicious anemia is expressed in U.S.P. Units.

TABLE OF U.S.P. XII INJECTIONS—CONTINUED

Official Latin Title, English Title and Synonym, if Any	*Brief Description*	*Prescribed Limits of Labeled Amount of Active Ingredients Including All Tolerances*
Injectio Histaminæ Phosphatis: Histamine Phosphate Injection (Liquor Histaminæ Phosphatis U.S.P. XI, Solution of Histamine Phosphate U.S.P. XI, Histamine Acid Phosphate Injection)	Sterile solution of 1 Gm. of Histamine Phosphate in enough water for injection to make 1000 cc. Sterilized preferably by Process C or F, U.S.P. XII, p. 614.	Contains 1 Gm. in 1000 cc.
Injectio Hydrargyri Salicylatis: Mercuric Salicylate Injection (Mercuric Salicylate Ampuls)	Sterile suspension in a suitable fixed oil.	Contains an amount of mercury (Hg) equivalent to 52.5–61 per cent of labeled amount of mercuric salicylate.
Injectio Insulini: Insulin Injection (Insulin, Insulin Hydrochloride)	An acidified aqueous solution of the active principle of the pancreas which affects the metabolism of glucose. Standardized so that each cc. contains either 20, 40, 80, or 100 U.S.P. Insulin Units.	95–105 per cent of potency stated on label; potency shall be expressed in U.S.P. Insulin Units which are equivalent in potency to the Unit declared on the label of the U.S.P. Zinc-Insulin Crystals Reference Standard.
Injectio Mercurophyllinæ: Mercurophylline Injection	Sterile solution in water for injection of sodium salt of β-methoxy-γ-hydroxy-mercuri propylamide of trimethyl cyclopentane dicarboxylic acid ($C_{14}H_{26}NO_5HgNa$) (the mercuri compound) and of theophylline in approximately molecular proportions.	Contains an amount of mercury equivalent to 37–42 per cent of labeled amount of the mercuri compound, and 93–107 per cent of labeled amount of theophylline ($C_7H_8N_4O_2.H_2O$).
Injectio Mersalylis et Theophyllinæ: Mersalyl and Theophylline Injection (Mersalyl and Theophylline Ampuls)	Sterile solution in water for injection of approximately 10 parts by weight of mersalyl ($C_{13}H_{16}HgNO_6Na$) to each 5 parts by weight of theophylline ($C_7H_8N_4O_2.H_2O$).	Contains mercury (Hg) equivalent to 37–42 per cent of labeled amount of mersalyl, and 93–107 per cent of labeled amount of theophylline.
Injectio Neostigminæ Methylsulfatis: Neostigmine Methylsulfate Injection (Neostigmine Methylsulfate Ampuls)	Sterile solution in water for injection.	90–110 per cent.
Injectio Ouabaini: Ouabain Injection (Ouabain Ampuls)	Sterile solution in water for injection.	Potency shall be stated on label in terms of quantity of U.S.P. Ouabain Reference Standard to which it is equivalent.

TABLE OF U.S.P. XII INJECTIONS—CONTINUED

Official Latin Title, English Title and Synonym if Any	*Brief Description*	*Prescribed Limits of Labeled Amount of Active Ingredients Including All Tolerances*
Injectio Parathyroidei Parathyroid Injection (Liquor Parathyroidei U.S.P. XI, Solution of Parathyroid, Parathyroid Extract)	Sterile solution in water for injection of the water-soluble principle or principles of the parathyroid glands which have the property of relieving the symptoms of parathyroid tetany and of increasing the calcium content of the blood serum in man and other animals.	One cc. possesses a potency of not less than 100 U.S.P. Parathyroid Units, each Unit representing 1/100 of the amount required to raise the calcium content of 100 cc. of the bood serum of normal dogs 1 mg. within 16–18 hours after administration.
Injectio Phenolsulfonphthaleini: Phenolsulfonphthalein Injection (Phenolsulfonphthalein Ampuls)	Sterile solution in isotonic solution of sodium chloride made with water for injection and rendered soluble with sodium bicarbonate or sodium hydroxide.	95–105 per cent of labeled amount of phenolsulfonphthalein. (Formula in U.S.P. calls for 6 Gm. of the drug in 1000 cc. of solution.)
Injectio Picrotoxini: Picrotoxin Injection	Sterile solution in isotonic solution of sodium chloride.	Contains in each cc. 90–110 per cent of labeled amount of picrotoxin.
Injectio Pituitarii Posterioris: Posterior Pituitary Injection (Liquor Pituitarii Posterioris U.S.P. XI, Solution of Posterior Pituitary U.S.P. XI, Solution of Pituitary)	Sterile solution in water for injection of the water-soluble principle or principles from the posterior lobe of the pituitary body of healthy domesticated animals used for food by man.	The potency shall be such that 0.1 cc. of Injection shall possess an activity equivalent to one U.S.P. Posterior Pituitary Unit (potency of 0.5 mg. of U.S.P. Posterior Pituitary Reference Standard).
Injectio Quininæ Hydrochloridi et Æthylis Carbamatis: Quinine Hydrochloride and Ethyl Carbamate Injection (Quinine Hydrochloride and Ethyl Carbamate Ampuls, Quinine-Urethane Injection)	Sterile solution in water for injection of approximately 2 parts of quinine hydrochloride and 1 part of ethyl carbamate.	95–105 per cent of labeled amount of quinine hydrochloride ($C_{20}H_{24}N_2O_2.HCl.2H_2O$) and of ethyl carbamate ($C_3H_7O_2N$).
Injectio Strophanthini: Strophanthin Injection (Strophanthin Ampuls)	Sterile solution in water for injection.	Potency shall be stated on label in terms of quantity of U.S.P. Ouabain Reference Standard to which it is equivalent.
Injectio Sulfobromophthaleini Sodici; Sulfobromophthalein Sodium Injecjection (Sulfobromophthalein Ampuls)	Colorless, or almost colorless, sterile solution of sulfobromophthalein sodium in water for injection.	94–106 per cent.
Injectio Theophyllinæ Æthylenediaminicæ: Theophylline Ethylenediamine Injection (Theophylline Ethylenediamine Ampuls, Aminophylline Ampuls)	Sterile solution in water for injection.	Contains an amount of anhydrous theophylline ($C_7H_8N_4O_2$) equivalent to 73–83 per cent of labeled amount of theophylline ethylenediamine.

LIGAMENTUM CARBASI ABSORBENS—Gauze Bandage

(Lig. Carbas. Absorb.—Roller Gauze Bandage)

Storage.—Packaged individually and sterilized in package. For further details, see U.S.P. XII, p. 255.

Summarized Description.

Prepared from Type I Absorbent Gauze in various widths and lengths; packaged in one continuous piece, tightly rolled and protected from contamination; must be sterile.

For *thread count* and other *tests,* see U.S.P. XII, pp. 254–255.

LIQUOR AMARANTHI—Solution of Amaranth

(Liq. Amaranth.)

Storage.—Preserve in tight, light-resistant containers.

Condensed Recipe.

Dissolve 1 Gm. of Amaranth in sufficient distilled water to make 100 cc.

Description.—Clear, vivid red liquid; slight odor. For further information, see U.S.P. XII, p. 259.

Remarks.—Solution of Amaranth which was previously official in N.F. VI is permitted for use as a coloring agent in foods, drugs and cosmetics under the Federal Food, Drug and Cosmetic Act. See Amaranth, p. 5. It is used to color Elixir of Phenobarbital U.S.P.

LIQUOR CHLORIDORUM TRIUM ISOTONICUS—Isotonic Solution of Three Chlorides

(Liq. Chlorid. Tri. Isoton.—Ringer's Solution)

Isotonic Solution of Three Chlorides contains, in each 100 cc., not less than 0.84 Gm. and not more than 0.88 Gm. of NaCl, not less than 25 mg. and not more than 35 mg. of KCl, and not less than 30 mg. and not more than 36 mg. of $CaCl_2.2H_2O$.

Unless otherwise specified, No. 3—Sterile Isotonic Solution of Three Chlorides for Parenteral Use must be dispensed.

Storage.—Preserve Sterile Solutions in hermetic or other suitable containers. See "Containers for Injections," U.S.P. XII, p. 567.

Condensed Recipe.

There are three Isotonic Solutions of Three Chlorides official. No. 1—Nonsterile Isotonic Solution of Three Chlorides is made by dissolving sodium chloride, 8.6 Gm.; potassium chloride, 0.30 Gm.; and calcium chloride, 0.33 Gm., in sufficient recently boiled distilled water to make 1000 cc. The resulting solution is filtered.

No. 2—Sterile Isotonic Solution of Three Chlorides Not for Parenteral Use is Solution No. 1 sterilized preferably by Process C, U.S.P. XII, p. 616.

No. 3—Sterile Isotonic Solution of Three Chlorides for Parenteral Use is Solution No. 1 in which the distilled water is replaced by water for injection and the solution sterilized preferably by Process C.

For details, see U.S.P. XII, pp. 261–263.

Description.—Clear, colorless solution; mild saline taste; pH 5–7.5. For *tests for purity* and *assays,* see U.S.P. XII, pp. 261–263.

Remarks.—This solution is claimed to be more compatible with blood and tissue than isotonic solution of sodium chloride. It may be used in place of water for injection in the preparation of injections. It is also used in the preparation of wet dressings and pastes for wounds and is used in all forms of dehydration, especially in cases in which gastro-intestinal secretions have been lost by vomiting, etc., so resulting in the decrease of sodium, calcium and potassium salts in the body. For general information see p. 212 of Principles of Pharmacy.

LIQUOR CHLOROAZODINI—Solution of Chloroazodin

(Liq. Chloroazodin.)

Solution of Chloroazodin contains, in each 100 cc., not less than 0.24 Gm. and not more than 0.28 Gm. of $C_2H_4Cl_2N_6$.

Caution.—Solution of Chloroazodin should not come in contact with metal.

Storage.—Preserve in tight, light-resistant containers.

Condensed Recipe.

Dissolve 2.6 Gm. of Choroazodin in sufficient glyceryl triacetate to make 1000 cc. using a dry vessel of glass or other vitreous material with a minimum exposure to air and light. After solution is effected close the vessel tightly and set aside for at least 30 days, filter and package immediately. For details, see U.S.P. XII, pp. 263–264.

Description.—Clear yellow liquid; somewhat oily; slight fatty odor; bitter taste; specific gravity 1.154–1.158.

For *identification, moisture* and *assay,* see U.S.P. XII, pp. 263–264.

Remarks.—The aqueous solution is not as stable as the solution in glyceryl triacetate. This solution is used similarly to those of the chloramines and hypochlorites in the dressing, packing or irrigating of infected wounds and cavities. See Chloroazodin, p. 11.

LIQUOR IODI—Solution of Iodine

(Liq. Iodi)

Solution of Iodine contains, in each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of iodine (I), and not less than 2.1 Gm. and not more than 2.6 Gm. of NaI.

Storage.—Preserve in tight containers, preferably at a temperature not above 35° C.

Condensed Recipe.

Dissolve 20 Gm. of iodine and 24 Gm. of sodium iodide in 50 cc. of distilled water, then add enough distilled water to make 1000 cc.

Description.—Transparent liquid; reddish brown color; odor of iodine. For *identification* and *assay,* see U.S.P. XII, pp. 269–270.

Remarks.—Used similarly to mild tincture of iodine as a skin disinfectant. It dries more slowly, however, as it does not contain any alcohol.

LIQUOR SODII CITRATIS ANTICOAGULANS—Anticoagulant Solution of Sodium Citrate

(Liq. Sod. Cit. Anticoag.)

Anticoagulant Solution of Sodium Citrate is a solution of sodium citrate in isotonic solution of sodium chloride and contains, in each 100 cc., not less than 2.3 Gm. and not more than 2.7 Gm. of sodium citrate ($Na_3C_6H_5O_7.2H_2O$), and not less than 0.85 Gm. and not more than 0.95 Gm. of sodium chloride (NaCl), including all tolerances.

Unless otherwise specified, No. 3—Sterile Anticoagulant Solution of Sodium Citrate for Parenteral Use must be dispensed.

Storage.—Preserve Sterile Solutions in hermetic or other suitable containers. See "Containers for Injections," U.S.P. XII, p. 567.

Condensed Recipe.

There are three Anticoagulant Solutions of Sodium Citrate official. No. 1—Non-sterile Anticoagulant Solution of Sodium Citrate is made by dissolving 25 Gm. of sodium citrate and 9 Gm. of sodium chloride in enough distilled water to make 1000 cc. and filtering.

No. 2—Sterile Anticoagulant Solution of Sodium Citrate Not for Parenteral Use is Solution No. 1 sterilized preferably by Process C, U.S.P. XII, p. 616.

No. 3—Sterile Anticoagulant Solution of Sodium Citrate for Parenteral Use is Solution No. 1 in which the distilled water is replaced by water for injection and the solution sterilized preferably by Process C. This solution may differ in sodium citrate content from that indicated on page 25 provided it meets certain requirements. For details, see U.S.P. XII, pp. 275–276.

Description.—Clear, colorless solution; slightly saline taste; pH 6.7–7.5. For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 275–276.

Remarks.—Used as an anticoagulant for the indirect transfusion of blood. It prevents the coagulation of the blood by calcium precipitation. Usually about 10 cc. of the solution is added to each 90 cc. to 100 cc. of whole blood and coagulation will not take place for about 48 hours. A sterile solution containing approximately 2.5 per cent of sodium citrate was formerly official in N.F. VI as Ampuls of Sodium Citrate.

LIQUOR TRIBROMOÆTHANOLIS—Solution of Tribromoethanol

(Liq. Tribromoæth.—Solution of Tribromoethyl Alcohol)

A solution of tribromoethanol in amylene hydrate containing, in each 100 cc., not less than 99 Gm. and not more than 101 Gm. of $C_2H_3Br_3O$.

Storage.—Preserve in tight, light-resistant containers, carefully dried prior to filling.

Condensed Recipe.

Dissolve 100 Gm. of tribromoethanol in 50 cc. of amylene hydrate, and add sufficient amylene hydrate to make 100 cc.

For use as an anesthetic 2.5 cc. of this solution is diluted with enough warm distilled water to make 100 cc. of the dilution. For details, see U.S.P. XII, pp. 277–278.

Description.—Clear, colorless liquid; camphoraceous odor; burning taste. For *tests* and *assay,* see U.S.P. XII, pp. 277–278.

Remarks.—Also known as avertin fluid. This solution is used for basal anesthesia by rectal administration in which case the amount of inhalation anesthetic needed to produce complete anesthesia is reduced. (Solution of Tribromoethyl Alcohol should not be used in dosage sufficient to produce complete anesthesia.) It is said to have the advantage of not producing irritation of the respiratory tract membranes and there is less tendency to nausea after operation. The solution has also been used in the control of certain convulsive conditions such as tetanus.

Dose.—For each kilogram of body weight, rectal, 0.06 cc. (1 minim).

Caution.—The total amount administered should not exceed 8 cc. for women or 10 cc. for men, regardless of weight.

MAGNESII PHOSPHAS TRIBASICUS—Tribasic Magnesium Phosphate

(Mag. Phos. Tribas.)

$Mg_3(PO_4)_2.5H_2O$ Molecular weight, 353.00

Tribasic Magnesium Phosphate, when ignited to constant weight, contains not less than 98 per cent of $Mg_3(PO_4)_2$.

Storage.—Preserve in well-closed containers.

Summarized Description.

White powder; odorless; tasteless; almost insoluble in water; readily soluble in diluted mineral acids.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 282–283.

Remarks.—Also known as "neutral" magnesium phosphate and tertiary magnesium phosphate. This is an antacid and is used in the treatment of peptic ulcer and of gastric hyperacidity. Being almost insoluble, it has an advantage over the alkaline hydroxides and alkali carbonates in that it neutralizes the excess acid in the stomach but does not induce alkalosis. It is also official in U.S.P. XII in the form of tablets.

Dose.—1 Gm. (15 grains).

MAGNESII TRISILICAS—Magnesium Trisilicate

(Mag. Trisil.)

$2MgO.3SiO_2.nH_2O$

Magnesium Trisilicate is a compound of magnesium oxide and silicon dioxide with varying proportions of water. It contains not less than 20 per cent of magnesium oxide (MgO), and not less than 45 per cent of silicon dioxide (SiO_2).

Storage.—Preserve in well-closed containers.

Summarized Description.

Fine, white powder, free from grittiness; odorless; tasteless; almost insoluble in water and alcohol; readily decomposed by mineral acids.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 284–286.

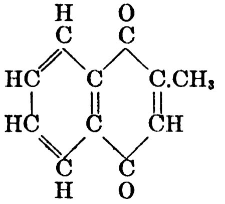
Remarks.—This is an antacid absorbent used in treatment of peptic ulcers and diarrhea. It readily absorbs odors. It reacts chemically with the hydrochloric acid in the stomach and does not produce systemic alkalization The tablets are also official in U.S.P. XII.

Dose.—1 Gm. (15 grains).

MENADIONUM—Menadione

(Menadion.—2-Methyl-Naphthoquinone)

$C_{11}H_8O_2$ Molecular weight, 172.17



Menadione, when dried over sulfuric acid in a vacuum desiccator for 4 hours, contains not less than 98.5 per cent of $C_{11}H_8O_2$.

Caution.—Menadione powder is irritating to the respiratory tract and to the skin, and an alcoholic solution has vesicant properties.

Storage.—Preserve in well-closed, light-resistant containers.

Summarized Description.

Bright yellow, crystalline powder; nearly odorless; affected by sunlight; practically insoluble in water; soluble in about 60 parts of alcohol, and in about 10 parts of benzene; moderately soluble in chloroform and in carbon tetrachloride; soluble in vegetable oils; melts 105°–107° C.

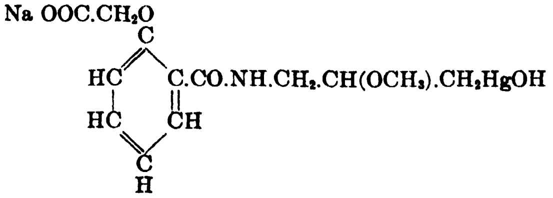
For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 288–289.

Remarks.—Menadione is a synthetic naphthoquinone derivative having the physiologic properties of Vitamin K, although it is not chemically identical with natural Vitamin K. There are actually two naturally occurring substances called Vitamin K_1 and Vitamin K_2, both of which have a naphthoquinone nucleus. Vitamin K is present in hog liver, hemp seed, tomatoes, cabbage, alfalfa and fish meal. Prothrombin is not synthesized in the liver if Vitamin K is not present, and Vitamin K, a fat-soluble vitamin, is not absorbed when the flow of bile is obstructed, so bile salts are administered along with it when prothrombin deficiency is due to bile obstruction. It is also of value in preventing and treating hemorrhagia neonatorum; preparations having Vitamin K activity are given to the mother during labor and sometimes parenterally to the newborn infant. The tablets are also official in U.S.P. XII.

Dose.—1 mg. (1/60 grain)

MERSALYL—Mersalyl

$C_{13}H_{16}HgNO_6Na$ Molecular weight, 505.87



Mersalyl, when dried over sulfuric acid for 24 hours, contains not less than 38.5 per cent and not more than 40.5 per cent of mercury (Hg).

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White or almost white, crystalline powder; odorless; bitter taste; somewhat deliquescent; gradually decomposed by light; soluble in about one part of water, and in about 2 parts of alcohol; insoluble in chloroform and in ether.

For *identification, tests for purity* and *assay* for mercury, see U.S.P. XII, pp. 291–292.

Remarks.—Also known as salyrgan. It is an antisyphilitic and principally a diuretic. Prescribed in ascites and edema, principally of cardiac and cardiorenal origin. It is injected intramuscularly together with theophylline, as the combination of the two drugs does not damage the tissue at the point of injection as sometimes happens when this organic mercurial is injected alone. The combination with theophylline is official in U.S.P. XII as Injectio Mersalylis et Theophyllinæ.

METHYLROSANILINÆ CHLORIDUM—Methylrosaniline Chloride

(Methylrosanil. Chlorid.—Gentian Violet, Methyl Violet, Crystal Violet)

Methylrosaniline Chloride is hexamethylpararosaniline chloride, usually admixed with pentamethylpararosaniline chloride and tetramethylpararosaniline chloride.

Storage.—Preserve in well-closed containers.

Summarized Description.

Dark green powder or greenish glistening pieces having a metallic luster; not more than a faint odor; soluble in 30 or 40 parts of water, in about 10 parts of alcohol, and in about 15 parts of glycerin; soluble in chloroform; insoluble in ether.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 294–295.

Remarks.—Formerly official in N.F. VI but transferred to U.S.P. by means of the Second Supplement to U.S.P. XI. It is a mixture of the methyl-pararosaniline chlorides but the hexamethyl compound predominates; the penta-methyl and the tetra-methyl compounds being unavoidable admixtures produced during the process of manufacture. It is an antiseptic, bactericide and anthelmintic and has selective action on gram-positive tissues. As it does not injure or irritate the tissues, it is used externally in surgery and also is used by veterinarians in the treatment of vaginal catarrh of cattle. It is also used intravenously in sterile solution in streptococcic infections. Solution of Methylrosaniline Chloride is official in N.F. VII.

Dose.—60 mg. (1 grain).

NEBULA EPINEPHRINÆ HYDROCHLORIDI—Epinephrine Hydrochloride Spray

(Nebul. Epineph. Hydrochlor.—Solution of Epinephrine Hydrochloride 1:100)

Epinephrine Hydrochloride Spray is a solution of epinephrine hydrochloride in distilled water and has a potency equivalent to a solution containing 1 Gm. of U.S.P. Epinephrine Reference Standard in each 100 cc.

Storage.—Preserve in small, well-filled, light-resistant, tight containers.

Summarized Description.

Nearly colorless liquid; slightly acid; gradually darkens on exposure to air and light. If solution becomes brown in color, or contains a precipitate, it must be rejected.

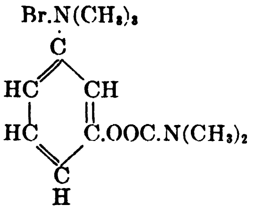
For *identification* see Liquor Epinephrinæ Hydrochloridi, U.S.P. XII, p. 266. For *assay* see Nebula Epinephrinæ Hydrochloridi, U.S.P. XII, p. 301.

Remarks.—This is used in severe attacks of asthma to relax bronchial spasm. This solution is ten times stronger than the official Solution of Epinephrine Hydrochloride and is not suitable for hypodermic injection but is used by oral inhalation.

NEOSTIGMINÆ BROMIDUM—Neostigmine Bromide

(Neostig. Bromid.)

$C_{12}H_{19}BrN_2O_2$ Molecular weight, 303.20



Neostigmine Bromide, when dried for 6 hours at 100° C., contains not less than 98 per cent of $C_{12}H_{19}BrN_2O_2$.

Storage.—Preserve in tight containers.

Summarized Description.

White, crystalline powder; odorless; bitter taste; soluble in about one part of water; soluble in alcohol; melts with decomposition at about 167° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 304.

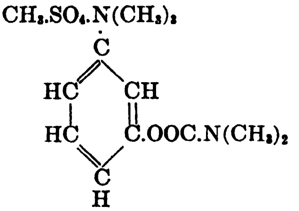
Remarks.—Also known as prostigmine bromide. Used especially in tablet form which is official in U.S.P. XII in oral treatment of myasthenia gravis. Also useful for prevention of atony of the intestinal and bladder musculature.

Dose.—Oral, 15 mg. (¼ grain).

NEOSTIGMINÆ METHYLSULFAS—Neostigmine Methylsulfate

(Neostig. Methylsulf.)

$C_{13}H_{22}N_2O_6S$ Molecular weight, 334.38



Neostigmine Methylsulfate, when dried at 100° C. for 6 hours, contains not less than 98 per cent of $C_{13}H_{22}N_2O_6S$.

Storage.—Preserve in tight containers.

Summarized Description.

White, crystalline powder; odorless; bitter taste; soluble in about 10 parts of water; less soluble in alcohol; melts 142°–145° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 305–306.

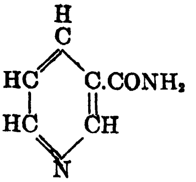
Remarks.—It is a miotic with an activity very similar to physostigmine. Also stimulates intestinal peristalsis and is used in postoperative intestinal paralysis to prevent distention. Like the bromide it is used in the treatment of myasthenia gravis. Neostigmine Methylsulfate Injection is also official in U.S.P. XII.

Dose.—Subcutaneous, 0.5 mg. (1/120 grain).

NICOTINAMIDUM—Nicotinamide

(Nicotinamid.—Nicotinic Acid Amide, Niacinamide)

$C_6H_6N_2O$ Molecular weight, 122.12



Nicotinamide, when dried over sulfuric acid for 18 hours, contains not less than 98.5 per cent of $C_6H_6N_2O$.

Storage.—Preserve in tight containers.

Summarized Description.

White, crystalline powder; odorless or nearly so; bitter taste; soluble in about one part of water, in about 1.5 parts of alcohol, and in about 10 parts of glycerin; melts 128°–131° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 306–307.

Remarks.—This is the amide of Nicotinic Acid (see p. 4). Used in the treatment of pellagra and is preferred in some cases because Nicotinic Acid oftens produces a histamine-like flush which is sometimes quite disturbing and this effect is much less pronounced with the use of the amide. The amide is also claimed not to produce as much vasomotor disturbance. It is also official in U.S.P. XII in the form of tablets. For general information, see Principles of Pharmacy, p. 905.

Dose.—25 mg. (3/8 grain).

OLEOVITAMINA A—Oleovitamin A

(Oleovitam. A—Natural Vitamin A in Oil)

Oleovitamin A is either fish liver oil, or fish liver oil diluted with an edible vegetable oil, or a solution of Vitamin A concentrate in fish liver oil or in an edible vegetable oil. The Vitamin A shall be obtained from natural (animal) sources. Oleovitamin A contains in each Gm. not less than 50,000 and not more than 65,000 U.S.P. Units of Vitamin A, and not more than 1000 U.S.P. Units of Vitamin D.

Storage.—Preserve in tight containers; may be bottled or packaged in containers from which the air has been expelled by the production of a vacuum or by an inert gas.

Summarized Description.

Thin, oily liquid; may have fishy, but not rancid, odor and taste.

For test for *free fatty acids* and *assay,* see U.S.P. XII, pp. 310–311.

Remarks.—This is a rich source of Vitamin A with a very small amount of Vitamin D. It is used in the treatment of Vitamin A deficiency diseases such as xerophthalmia, nyctalopia (night-blindness), follicular keratosis, etc. Deficiency of Vitamin A also results in lowered resistance of the body to infection in general and retardation of growth. Oleovitamin A has an advantage over cod liver oil, especially in the treatment of the deficiency diseases where large doses are required, in that a much smaller amount is necessary to provide the required units of Vitamin A and a much smaller amount of Vitamin D is present. Five drops of Oleovitamin A are approximately equivalent to 2 teaspoonfuls of cod liver oil in its Vitamin A content. The capsules are also official in U.S.P. XII.

Dose.—Prophylactic, infants and adults, 0.1 cc. (1½ minims).

OLEOVITAMINA A ET D—Oleovitamin A and D

(Oleovitam. A et D)

Oleovitamin A and D is either fish liver oil, or fish liver oil diluted with an edible vegetable oil, or a solution of Vitamin A and D concentrates in fish liver oil or in an edible vegetable oil. The Vitamin A shall be obtained from natural (animal) sources and the Vitamin D may be obtained from natural (animal) sources or may be synthetic Oleovitamin D. Oleovitamin A and D contains in each Gm. not less than 850 and not more than 1100 U.S.P. Units of Vitamin A, and not less than 85 and not more than 110 U.S.P. Units of Vitamin D.

Oleovitamin A and D may be flavored by the addition of not more than 1 per cent of any one or any mixture of flavoring substances recognized in the Pharmacopœia.

Storage.—Preserve in tight containers. It may be bottled or packaged in containers from which the air has been expelled by the production of a vacuum or by an inert gas.

Summarized Description.

Thin, oily liquid; may have a fishy, but not rancid, odor and taste; slightly soluble in alcohol; miscible in all proportions with ether and with chloroform.

For *tests for purity* and *assays,* see U.S.P. XII, p. 311.

Remarks.—Used in cases where mixed fat-soluble vitamin deficiencies are present and where both Vitamin A and Vitamin D are desired. This preparation is intended as a substitute for cod liver oil (the supply of which is uncertain at the present time) as far as Vitamin A and Vitamin D content are involved. The dosage is the same as that of cod liver oil and as its potency is fixed it may be more uniform than that of cod liver oil on which only minimum requirements are set.

Dose.—Infants and adults, 8 cc. (2 fluidrachms).

OLEOVITAMINA A ET D CONCENTRATA—Concentrated Oleovitamin A and D

(Oleovitam. A et D. Conc.)

Concentrated Oleovitamin A and D is either fish liver oil, or fish liver oil diluted with an edible vegetable oil, or a solution of Vitamin A and D concentrates in fish liver oil or in an edible vegetable oil. The Vitamin A shall be obtained from natural (animal) sources and the Vitamin D may be obtained from natural (animal) sources or may be synthetic oleovitamin D. Concentrated Oleovitamin A and D contains in each Gm. not less than 50,000 and not more than 65,000 U.S.P. Units of Vitamin A, and not less than 10,000 and not more than 13,000 U.S.P. Units of Vitamin D.

Storage.—Preserve in tight containers; may be bottled or packaged in containers from which the air has been expelled by the production of a vacuum or by an inert gas.

Summarized Description.

Thin, oily liquid; may have a fishy, but not rancid, odor and taste.

For *tests for purity* and *assays,* see U.S.P. XII, p. 312.

Remarks.—Provides a highly concentrated source of Vitamin A and of Vitamin D and is used for both the prophylaxis and the treatment of conditions requiring both vitamins. The dose of 5 drops contains approximately the same amount of Vitamins A and D as is contained in 2 teaspoonfuls of cod liver oil. This preparation is also official in U.S.P. XII as capsules.

Dose.—Prophylactic, infants and adults, 0.1 cc. (1½ minims).

OLEUM CEDRI FOLII—Oil of Cedar Leaf

(Ol. Ced. Fol.—Oil of Arbor Vitæ, Oil of Thuja)

Oil of Cedar Leaf is the volatile oil distilled with steam from the fresh leaves of *Thuja occidentalis* Linné (Fam. *Pinaceœ*). Oil of Cedar Leaf contains not less than 60 per cent of ketones, calculated as thujone ($C_{10}H_{16}O$).

Storage.—Preserve in well-filled, tight containers and avoid exposure to excessive heat.

Summarized Description.

Colorless or yellow liquid; characteristic odor of arbor vitæ; soluble in 3 volumes of 70 per cent alcohol; specific gravity 0.910–0.920 at 25° C.; optical rotation in 100-mm. tube at 25° C. −10° to −13°; refractive index 1.4560–1.4590 at 20° C.

For *assay,* see U.S.P. XII, p. 317.

Remarks.—Also known as oil of white cedar. Has been used as an emmenagogue, expectorant, antirheumatic and anthelmintic. Also used in skin diseases but principal use is for its odor. It was introduced into the Second Supplement of U.S.P. XI. It may be used in Liniment of Soft Soap in place of Oil of Lavender.

OLEUM HIPPOGLOSSI—Halibut Liver Oil

(Ol. Hippoglos.)

Halibut Liver Oil is the fixed oil obtained from the fresh, or suitably preserved livers of *Hippoglossus hippoglossus* Linné (Fam. *Pleuronectidæ*). Halibut Liver Oil contains in each Gm. not less than 60,000 U.S.P. Units of Vitamin A and not less than 600 U.S.P. Units of Vitamin D.

The Vitamin A potency and Vitamin D potency of Halibut Liver Oil, when designated on the label, shall be expressed in "United States Pharmacopœia Units" per Gm. of oil and may be referred to as "U.S.P. Units."

Halibut Liver Oil may be flavored by the addition of not more than 1 per cent of any one or any mixture of flavoring substances recognized in the Pharmacopœia.

Storage.—Preserve in tight containers; may be bottled or packaged in containers from which the air has been expelled by the production of a vacuum or by an inert gas.

Summarized Description.

Yellow to brownish yellow, oily liquid; slightly fishy, but not rancid, odor; fishy taste; insoluble in water; slightly soluble in alcohol; freely soluble in ether, in chloroform, in carbon disulfide, and in ethyl acetate; specific gravity 0.920–0.930.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 322–323.

Remarks.—This is another preparation with a high Vitamin A potency, but with a rather small Vitamin D content. For further information, see "Remarks" under Oleovitamina A on p. 30, as the two products are very similar in their vitamin content. The capsules are also official in U.S.P. XII.

Dose.—Prophylactic, infants and adults, 0.1 cc. (1½ minims). If the Vitamin A content exceeds the minimum requirements, proportionally smaller doses may be given.

OLEUM PERSICÆ—Persic Oil

(Ol. Persic.—Apricot Kernel Oil, Peach Kernel Oil)

Persic Oil is the oil expressed from the kernels of varieties of *Prunus Armeniaca* Linné (Fam. *Rosaceæ*) (Apricot Kernel Oil), or from the kernels of varieties of *Prunus Persica* Sieb. et Zucc. (Fam. *Rosaceæ*) (Peach Kernel Oil).

Persic Oil must be labeled to indicate whether it was derived from apricot kernels or from peach kernels.

Storage.—Preserve in tight containers.

Summarized Description.

Clear, pale straw-colored or colorless, oily liquid; almost odorless; bland taste; slightly soluble in alcohol; miscible with ether, chloroform, benzene, and purified benzin; specific gravity 0.910–0.918.

For *tests for purity,* see U.S.P. XII, p. 333.

Remarks.—Used as an emollient and in ointments. Introduced into Supplement II of U.S.P. XI. In the formula for Rose Water Ointment, the Expressed Oil of Almond may be replaced by an equal weight of Persic Oil.

OUABAINUM—Ouabain

(Ouabain.—G-Strophanthin)

$C_{29}H_{44}O_{12}.8H_2O$ Molecular weight, 728.77

Ouabain is a glycoside occurring in *Acokanthera Ouabaio* Arnaud and obtained from the seeds of *Strophanthus gratus* (Wall. et Hook.) Baillon (Fam. *Apocynaceæ*).

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White, odorless crystals, or crystalline powder; stable in air but affected by light; soluble slowly in about 75 parts of water, and in about 100 parts of alcohol at 25° C.; more soluble in hot water and in hot alcohol; melts 186°–189° C. (for conditions, see U.S.P. XII); specific rotation [α] under specified conditions (see U.S.P.) –31° to –32.5°. It is extremely poisonous.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 341–342.

Remarks.—It is a cardiac stimulant similar to strophanthin; its action is rapid and it has a lesser tendency than digitalis to cumulative action. Injectio Ouabaini is also official in U.S.P. XII.

Dose.—Intravenous, 0.25 mg. (1/250 grain).

PAMAQUINÆ NAPHTHOAS—Pamaquine Naphthoate

(Pamaquin. Naphth.—Aminoquin Naphthoate)

$C_{42}H_{45}N_3O_7$ Molecular weight, 703.8

Pamaquin naphthoate is the methylene-bis-β-hydroxynaphthoate of 6-methoxy-8-(1-methyl-4-diethylamino) butylaminoquinoline. It contains, when dried at 100° C. for 6 hours, not less than 43 per cent and not more than 45 per cent of 6-methoxy-8-(1-methyl-4-diethylamino) butylaminoquinoline (pamaquine base) and not less than 53 per cent and not more than 57 per cent of methylene-bis-β-hydroxynaphthoic acid.

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

Yellow to orange powder; odorless; tasteless, or nearly so; has a local anesthetic effect when placed on tongue; insoluble in water; soluble in alcohol and in acetone.

For *identification* and *assays* for its constituents, see U.S.P. XII, pp. 345–346.

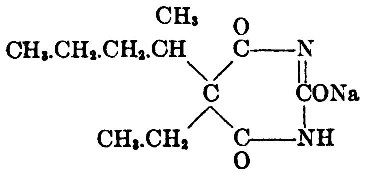
Remarks.—Also known as plasmochin. It is an antimalarial which has an advantage over quinine in that it destroys the gametes or sexual forms of the malarial parasite. It is not used as a substitute for quinine, however, but is used with it, as it cannot be used for long periods of time as a prophylactic because of possible toxic action.

Dose.—20 mg. (1/3 grain).

PENTOBARBITALUM SODICUM—Pentobarbital Sodium

(Pentobarb. Sod.—Pentobarbitalum Solubile U.S.P. XI, Soluble Pentobarbital U.S.P. XI)

$C_{11}H_{17}N_2O_3Na$ Molecular weight, 248.26



Pentobarbital Sodium contains not less than 90 per cent and not more than 92 per cent of pentobarbital ($C_{11}H_{18}N_2O_3$), calculated on a moisture-free basis, the moisture being determined on a separate portion by drying at 90° C. for 6 hours.

Storage.—Preserve in tight containers.

Summarized Description.

White, crystalline granules, or white powder; odorless; slightly bitter taste; very soluble in water; freely soluble in alcohol; practically insoluble in ether.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 349–350.

Remarks.—Also known as nembutal and embutal. First introduced into U.S.P. by means of Second Supplement to U.S.P. XI. It is a rapidly acting hypnotic and sedative which is effective in smaller doses than barbital but its action lasts only for a relatively short time. It is used as a sedative particularly before local, general or spinal anesthesia. It is preferably administered orally or by rectum but in some cases may be injected intravenously. Both capsules and tablets of pentobarbital sodium are official in U.S.P. XII.

Dose.—0.1 Gm. (1½ grains).

PERPOLITIONES ORYZÆ—Rice Polishings

(Perpol. Oryz.—Rice Bran, Tikitiki)

Rice Polishings consist of the fine, flaky pericarp and spermoderm fragments, the embryo, aleurone layer, and outer adhering cells of the starchy endosperm of the grain of *Oryza sativa* Linné (Fam. *Gramineæ*).

Rice Polishings contain not more than 40 per cent of starch and not more than 10 per cent of rice hull or other foreign matter.

Storage.—Preserve in well-closed containers and against attack by insects. (See U.S.P., p. 5.)

Summarized Description.

Fine, flaky, yellowish white to pale orange powder; non-rancid odor; sweetish taste.

For *histology, test for rice hull or other foreign matter, identification* and *test for starch,* see U.S.P. XII, pp. 350–351.

Remarks.—Raw material from which Extract of Rice Polishings is made. See p. 17.

PICROTOXINUM—Picrotoxin

(Picrotox.—Cocculin)

Picrotoxin is a glycoside obtained from the seed of *Anamirta paniculata* Colebrooke (Fam. *Menispermaceæ*).

Storage.—Preserve in well-closed, light-resistant containers.

Summarized Description.

Flexible, shining, prismatic crystals or as a microcrystalline powder; odorless; stable in air; affected by light; soluble in about 350 parts of water, in about 5 parts of boiling water, in about 3 parts of boiling alcohol; more readily soluble in diluted acids and alkalies; sparingly soluble in ether and in chloroform; melts 198°–200° C.

For *identification* and *tests for purity,* see U.S.P. XII, p. 363.

Remarks.—This was the first amaroid discovered and is an anhidrotic used especially in treatment of night sweats in tuberculosis. It also has been used in chorea and chronic alcoholism and in ointment form as a parasiticide, although this is a dangerous use of this poison. It was introduced into the U.S.P. because of its value as a quite effective antidote for barbiturate poisoning. Injectio Picrotoxini is also official in U.S.P. XII. For further information, see Principles of Pharmacy, p. 879

Dose.—2 mg. (1/30 grain) or more, depending on the severity of the barbiturate poisoning.

PLASMA HUMANUM NORMALE CITRATUM—Citrated Normal Human Plasma

(Plas. Human. Nor. Citr.—Normal Human Plasma)

Citrated Normal Human Plasma is the sterile plasma obtained by pooling approximately equal amounts of the liquid portion of citrated whole blood from eight or more humans (*Homo sapiens*) who have been certified by a qualified doctor of medicine as free from any disease which is transmissible by blood transfusion at the time of drawing the blood. Citrated Normal Human Plasma complies with the requirements of the National Institute of Health of the United States Public Health Service. For details of the bleeding and preparation, see U.S.P. XII. The plasma may be dispensed as liquid, frozen or dried plasma.

Storage.—Preserve liquid plasma between 15° and 30° C., frozen plasma at or under −15° C., and do not expose dried plasma to excessive heat; must be dispensed in the manufacturer's original unopened glass container.

Summarized Description.

Freshly collected citrated human plasma is a slightly opalescent liquid; faint yellowish or amber color; practically odorless unless preservative with odor used. To make frozen plasma this liquid is frozen quickly, within 72 hours of bleeding, and under conditions to avoid formation of a solid mass. Dried plasma is made from frozen plasma without added dextrose (sometimes added as stabilizing agent) by drying from the frozen state under vacuum. It has a light yellow to deep cream color and is restored to original volume by dissolving completely in Water for Injection, and is administered immediately.

For details of *description* and *regulations*, see U.S.P. XII, pp. 367–368.

Remarks.—Human plasma is administered in the treatment of surgical and traumatic shock and in the treatment of burns where there has been loss of available plasma. It is far superior to salt or dextrose solutions for such purposes. It is also injected as a temporary substitute for whole blood in the treatment of hemorrhage when whole blood is not immediately available and when red blood corpuscles are not immediately needed.

Dose.—Intravenous, 500 cc.

POTASSII CHLORIDUM—Potassium Chloride

(Pot. Chlorid.)

KCl Molecular weight, 74.55

Potassium Chloride, when dried for 4 hours at 110° C., contains not less than 99 per cent of KCl.

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless, elongated, prismatic, or cubical crystals, or white, granular powder; odorless; saline taste; permanent in air; soluble in 2.8 parts of water and in about 2 parts of boiling water; insoluble in alcohol.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 373–374.

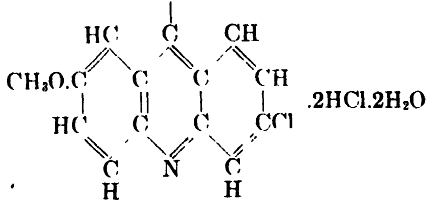
Remarks.—Formerly official in N.F. VI. Has been used in fever and in epilepsy. Introduced into U.S.P. XII as a diuretic for edematous patients, especially those with chronic nephritis, in whom the usual diuretics are not effective. It is an ingredient of Isotonic Solution of Three Chlorides and is also official in U.S.P. XII in the form of tablets.

Dose.—1 Gm. (15 grains).

QUINACRINÆ HYDROCHLORIDUM—Quinacrine Hydrochloride

(Quinacrin. Hydrochlor.—Mepacrine Hydrochloride)

$C_{23}H_{30}ClN_3O.2HCl.2H_2O$ Molecular weight, 508.91



Quinacrine Hydrochloride contains not less than 77 per cent and not more than 80.2 per cent of quinacrine base, $C_{23}H_{30}ClN_3O$, corresponding to not less than 98 per cent of $C_{23}H_{30}ClN_3O.2HCl.2H_2O$.

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

Bright yellow, crystalline powder; odorless; bitter taste; soluble in about 35 parts of water; soluble in alcohol.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 383–384.

Remarks.—Also known as atabrine dihydrochloride and as chinacrin dihydrochloride. It is used in the prophylaxis and treatment of malaria and like quinine destroys the asexual forms of the causative organism. It is an acridine dye and stains the tissues of the patient yellow. It differs from quinine in that it is excreted slowly and often a course of treatment is not repeated for a month or two. The tablets are also official in U.S.P. XII.

Dose.—0.1 Gm. (1½ grains).

QUININÆ HYDROCHLORIDUM—Quinine Hydrochloride

(Quin. Hydrochlor.)

$C_{20}H_{24}N_2O_2.HCl.2H_2O$ Molecular weight, 396.91

The hydrochloride of an alkaloid obtained from cinchona.

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White, silky, glistening needles; odorless; bitter taste; effloresces when exposed to warm air; soluble in 16 parts of water, in 1 part of alcohol, in about 7 parts of glycerin, in about 1 part of chloroform, in about 350 parts of ether, and in about 0.5 part of boiling water.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 389–390.

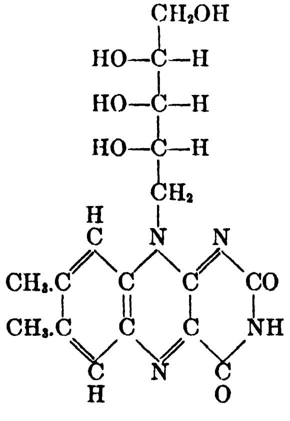
Remarks.—Formerly official in N.F. VI. Also known as quinine chloride, hydrochlorate, or muriate. This salt of quinine is more soluble than the sulfate and is well adapted for intravenous injection. It is an antimalarial, antipyretic, antiseptic and bitter tonic. It is also extensively used in veterinary medicine. The tablets are also official in U.S.P. XII and it is an ingredient in Injectio Quininæ Hydrochloridi et Æthylis Carbamatis. Quinine and salts of quinine may be sold only for the treatment of malaria under recent regulations of the War Production Board.

Dose.—0.2 Gm. (3 grains).

RIBOFLAVINUM—Riboflavin

(Riboflav.—Lactoflavin, Vitamin B_2, Vitamin G)

$C_{17}H_{20}N_4O_6$ Molecular weight, 376.36



Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

Orange yellow, crystalline powder; slight odor; deteriorates rapidly in solution, especially in the presence of alkalies, the deterioration being accelerated by light;

not appreciably affected by diffused light when in dry state; soluble in about 10,000 parts of water; more soluble in isotonic solution of sodium chloride; less soluble in alcohol; insoluble in ether and in chloroform; very soluble in dilute alkalies; melts with decomposition at about 280° C., the bath being preheated to 250° C.; specific rotation $[\alpha]_D^{25}$ is —112° to —122° when determined under certain specified conditions. (See U.S.P. XII.)

For *identification* and *tests for purity,* see U.S.P. XII, pp. 393–394.

Remarks.—This is one of the Vitamin B complex factors and is stable to heat. It is recognized as a specific in the treatment of certain characteristic lesions of the tongue, the lips, and the face. A deficiency of this factor also causes certain ocular manifestations. It is administered in cases of pellagra which are resistant to nicotinic acid therapy. The tablets are also official in U.S.P. XII.

Dose.—5 mg. (1/12 grain).

SERUM HUMANUM NORMALE—Normal Human Serum

(Ser. Human. Nor.—Human Serum)

Normal Human Serum is the sterile serum obtained by pooling approximately equal amounts of the liquid portion of coagulated whole blood from eight or more humans (*Homo sapiens*) who have been certified by a qualified doctor of medicine as free from any disease which is transmissible by blood transfusion at the time of drawing the blood. Normal Human Serum complies with the requirements of the National Institute of Health of the United States Public Health Service. For details of bleeding and preparation of the serum, see U.S.P. XII, pp. 404–405.

Storage.—Preserve liquid serum at temperature of 2°–10° C.; do not expose dried serum to excessive heat; must be dispensed in the manufacturer's original unopened container.

Summarized Description.

May be dispensed in liquid or dried state. Freshly collected Normal Human Serum is a slightly opalescent liquid; faint yellowish or amber color; practically odorless unless preservative with odor added. The dried serum is made by freezing quickly, under conditions to avoid the formation of a solid mass, the liquid serum within 24 hours from separation from clot, and then drying the frozen serum under vacuum. It is a light yellow to deep cream color.

For details of *description* and for *regulations,* see U.S.P. XII, pp. 404–405.

Remarks.—Normal Human Serum has uses similar to those of Citrated Normal Human Plasma (See p. 34.)

Dose.—Intravenous, 500 cc.

SERUM IMMUNE MORBILLOSI HUMANUM—Human Measles Immune Serum

(Ser. Immun. Morbill. Human.—Measles Convalescent Serum)

Human Measles Immune Serum is sterile serum obtained from the blood of a healthy human (*Homo sapiens*) who has survived an attack of measles. Human Measles Immune Serum complies with the requirements of the National Institute of Health of the United States Public Health Service.

Storage.—Preserve at a temperature of 2°–10° C., preferably at lower limit; must be dispensed from manufacturer's original unopened glass container.

Summarized Description.

Transparent or slightly opalescent liquid; faint brownish, yellowish, or greenish color; nearly odorless or having an odor due to the presence of a preservative; may have slight granular deposit.

For further *description* and *regulations,* see U.S.P. XII, pp. 405–406.

Remarks.—It is administered during the incubation period to prevent or modify an expected attack of measles.

Dose.—Parenteral, therapeutic, 20 cc.; prophylactic, 10 cc.

SERUM IMMUNE SCARLATINÆ HUMANUM—Human Scarlet Fever Immune Serum

(Ser. Immun. Scarlat. Human.—Scarlet Fever Convalescent Serum)

Human Scarlet Fever Immune Serum is a sterile serum obtained from the blood of a healthy human (*Homo sapiens*) who has survived an attack of scarlet fever. Human Scarlet Fever Immune Serum complies with the requirements of the National Institute of Health of the United States Public Health Service.

Storage.—Preserve at a temperature of 2°–10° C., preferably at the lower limit; must be dispensed from manufacturer's original unopened glass container.

Summarized Description.

Transparent or slightly opalescent liquid; faint brownish, yellowish, or greenish color; nearly odorless or having odor due to preservative added; may have slight granular deposit.

For further *description* and *regulations*, see U.S.P. XII, p. 406.

Remarks.—This serum is injected to transfer passive immunity to a person exposed to scarlet fever.

Dose.—Parenteral, therapeutic, 20 cc.; prophylactic, 10 cc.

SODII SULFIS EXSICCATUS—Exsiccated Sodium Sulfite

(Sod. Sulfis. Exsicc.)

Na_2SO_3 Molecular weight, 126.05

Exsiccated Sodium Sulfite contains not less than 95 per cent of Na_2SO_3.

Storage.—Preserve in well-closed containers.

Summarized Description.

White powder; odorless; cooling, saline, sulfurous taste; oxidizes in air; soluble in about 4 parts of water; sparingly soluble in alcohol.

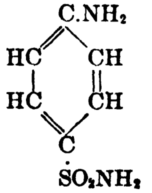
For *identification, tests for purity* and *assay*, see U.S.P. XII, pp. 422–423.

Remarks.—Exsiccated Sodium Sulfite has been introduced into U.S.P. XII as a preservative. It is used for this purpose in tannic acid ointment. It is an antiseptic and antizymotic and has been used internally in fermentative dyspepsia; it has been used externally in parasitic skin diseases and industrially has been used in preserving meat, egg yolk and other food products. The use in foods as a preservative is subject to stringent regulations and is generally prohibited.

SULFANILAMIDUM—Sulfanilamide

(Sulfanilamid.)

$C_6H_8N_2O_2S$ Molecular weight, 172.20



Sulfanilamide, when dried at 100° C. for 4 hours, contains not less than 99 per cent of $C_6H_8N_2O_2S$.

Storage.—Preserve in well-closed, light-resistant containers.

Summarized Description.

White crystals, granules, or powder; odorless; affected by light; soluble in about 125 parts of water, in about 37 parts of alcohol, and in about 5 parts of acetone; soluble in glycerin, in hydrochloric acid, and in aqueous solutions of potassium and sodium hydroxides; very soluble in boiling water; insoluble in chloroform, in ether, and in benzene; melts 164.5°–166.5° C.

For *identification, tests for purity* and *assay*, see U.S.P. XII, pp. 438–439.

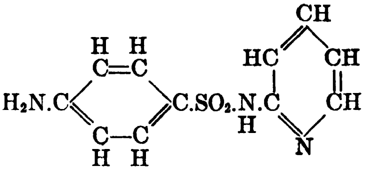
Remarks.—Also known as prontosil album, stramid, streptocid, deseptyl, sulphonamide P, sulfamidyl, p-aminobenzenesulfonamide, and p-aminophenylsulfonamide. First became official in the Second Supplement to U.S.P. XI. It is made by the reaction between acetanilid and chlorosulfonic acid, the resulting chlorosulfone being treated with ammonia, and then removing the acetyl group by hydrolysis with acid. It is an anti-infective and is effective against hemolytic streptococcic and meningococcic infections, gonococcic infections, and certain urinary infections. The tablets are also official in U.S.P. XII.

Dose.—2 Gm. (30 grains).

SULFAPYRIDINUM—Sulfapyridine

(Sulfapyridin.)

$C_{11}H_{11}N_3O_2S$ Molecular weight, 249.28



Sulfapyridine, when dried at 100° C. for 4 hours, contains not less than 99 per cent of $C_{11}H_{11}N_3O_2S$.

Storage.—Preserve in well-closed, light-resistant containers.

Summarized Description.

White or faintly yellowish white crystals, granules, or powder; odorless or nearly so; stable in air; slowly darkens on exposure to light; soluble in about 3500 parts of water, in about 440 parts of alcohol, and in about 65 parts of acetone; freely soluble in dilute mineral acids and in aqueous solutions of potassium and sodium hydroxides; melts 191°–193° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 439–440.

Remarks.—Also known as 2-sulfanilyl aminopyridine and dagenan. Used in the treatment of pneumococcic pneumonia and other pneumococcic infections; also used in the treatment of gonococcic infections. Sulfapyridine tablets are also official in U.S.P. XII.

Dose.—2 Gm. (30 grains).

SULFAPYRIDINUM SODICUM STERILE—Sterile Sulfapyridine Sodium

(Sulfapyridin. Sod. Steril.—Sterile Sodium Sulfapyridine)

$C_{11}H_{10}N_3O_2SNa.H_2O$ Molecular weight, 289.29

Sterile Sulfapyridine Sodium, when dried at 105° C. for 4 hours, contains not less than 99 per cent of anhydrous $C_{11}H_{10}N_3O_2SNa$. It meets the requirements of the "Sterility Tests for Solids," U.S.P. XII, p. 610.

Storage.—Preserve in containers so closed that the sterility of the product is maintained until the package is opened for use. No more than 10 Gm. may be placed in container but container may be of such size as to permit solution within the container. For *label requirements* and other *details,* see U.S.P. XII.

Summarized Description.

White crystals or powder; odorless; affected by light; absorbs carbon dioxide upon prolonged exposure to humid air and liberates sulfapyridine, becoming incompletely soluble in water; soluble in about 1.5 parts of water and in about 10 parts of alcohol.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 440–441.

Remarks.—This is used in the preparation of solutions for intravenous use. See Sufapyridine for uses.

Dose.—2 Gm. (30 grains).

SULFARSPHENAMINA—Sulfarsphenamine

(Sulfarsphen.)

Sulfarsphenamine consists chiefly of disodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-*N*-dimethylenesulfonate. It contains not less than 19 per cent of Arsenic (As).

Sulfarsphenamine must be prepared in an establishment licensed for the purpose by the United States Government upon recommendation of the Surgeon General of the United States Public Health Service. Each lot of the product before being offered for sale must comply with the toxicity, labeling, and other requirements of the National Institute of Health, and be released by the Institute.

Storage.—Preserve in a cool place, preferably not above 20° C., in sealed tubes of colorless glass, from which the air has been excluded either by the production of a vacuum or by displacement with a non-oxidizing gas.

Summarized Description.

Yellow powder; odorless or has a very slight odor resembling sulfur dioxide; slowly oxidized by exposure to air in dry state or in solution, becoming dark and more toxic; very soluble in water yielding a yellow solution; slightly soluble in alcohol; insoluble in ether.

For *identification, tests for purity, required labeling on container* and *assay,* see U.S.P. XII, pp. 441–442.

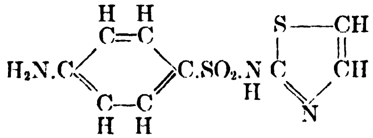
Remarks.—This drug is a spirillicide. In cases where it is not feasible to carry out intravenous treatment with arsphenamine and neoarsphenamine, especially in children, Sufarsphenamine can be injected intramuscularly. It is used in treatment of heredosyphilis.

Dose.—Intramuscular, 0.45 Gm. (7 grains).

SULFATHIAZOLUM—Sulfathiazole

(Sulfathiazol.)

$C_9H_9N_3O_2S_2$ Molecular weight, 255.31



Sulfathiazole, when dried at 100° C. for 4 hours, contains not less than 99 per cent of $C_9H_9N_3O_2S_2$.

Storage.—Preserve in well-closed, light-resistant containers.

Summarized Description.—White or faintly yellowish white crystals, granules or powder; odorless or nearly so; stable in air; slowly darkens on exposure to light; soluble in about 1700 parts of water, and in about 200 parts of alcohol; soluble in acetone; freely soluble in diluted mineral acids, in aqueous solutions of potassium and sodium hydroxides, and in ammonia T.S.; melts 200°–204° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 443–444.

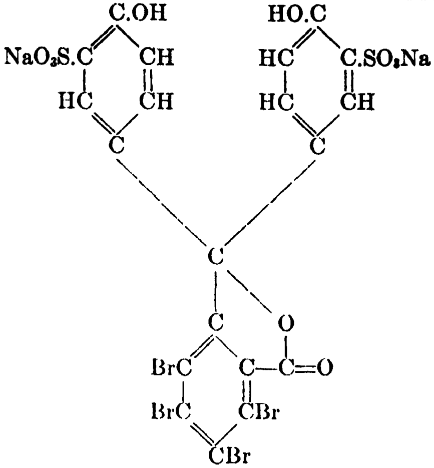
Remarks.—Also known as 2-sulfanilamidothiazole and 2-sulfanilylaminothiazole. It may be prepared by the condensation of p-acetylaminobenzenesulfonylchloride with 2-aminothiazole in pyridine. Upon diluting the reaction mixture with water a compound separates out which is hydrolyzed with hydrochloric acid. The acid solution is then neutralized to congo red and the resulting sulfathiazole is recrystallized from alcohol. It is administered orally in the treatment of pneumococcic pneumonia and is also used along with surgical measures in the treatment of staphylococcic infections. It is also preferably used in the treatment of male gonorrhea. It is also official in the form of tablets in U.S.P. XII.

Dose.—2 Gm. (30 grains).

SULFOBROMOPHTHALEINUM SODICUM—Sulfobromophthalein Sodium

(Sulfobromophthal. Sod.)

$C_{20}H_8Br_4O_{10}S_2Na_2$ Molecular weight, 838.04



Storage.—Preserve in tight containers.

Summarized Description.

White, crystalline powder; odorless; bitter taste; hygroscopic; soluble in water; insoluble in alcohol and in acetone.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 444–445.

Remarks.—Used in the preparation of the injection which is official in U.S.P. XII. Sulfobromophthalein Sodium injection is administered to test liver function.

SYRUPUS GLYCYRRHIZÆ—Syrup of Glycyrrhiza

(Syr. Glycyrrh.—Syrup of Licorice)

Storage.—Preserve in well-closed containers, preferably at a temperature not above 25° C.

Alcohol Content.—From 5 to 6 per cent, by volume.

Condensed Recipe.

Add 0.05 cc. of Oil of Fennel and 0.5 cc. of Oil of Anise to 250 cc. of Fluidextract of Glycyrrhiza and mix thoroughly; then add enough Syrup to make 1000 cc. This monograph appears on p. 453 of U.S.P. XII.

Remarks.—This is a vehicle which was formerly official in N.F. VI. It is a pleasant vehicle for bitter substances.

TABELLÆ—Tablets

The monograph for Tablets of Glyceryl Trinitrate was the only tablet monograph appearing in U.S.P. XI with the exception of the monographs on poison tablets of mercury bichloride which also appear in U.S.P. XII as "Toxitabellæ." There are 49 monographs on tablets in U.S.P. XII, 47 of which are new additions. Erythrityl tetranitrate tablets appeared in U.S.P. XI as Diluted Erythrityl Tetranitrate and many of the new tablet monographs previously appeared in N.F. VI. For general information on *compressed tablets,* see Principles of Pharmacy, pp. 344–346.

Following is a table in which are listed all of the tablets which are official in U.S.P. XII with pertinent information about each. For further information and for *identification, tests for purity, assay, storage* and *dose,* see U.S.P. XII, pp. 457–492

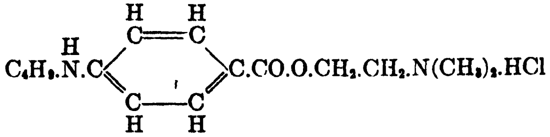
Latin Title	*English Title and Synonym, if Any*	*Prescribed Limits of Labeled Amount of Active Ingredients Including All Tolerances*
Tabellæ Acetophenetidini	Acetophenetidin Tablets (Phenacetin Tablets)	94–106 per cent
Tabellæ Acidi Acetylsalicylici	Acetylsalicylic Acid Tablets (Aspirin Tablets)	95–105 per cent
Tabellæ Acidi Ascorbici	Ascorbic Acid Tablets (Vitamin C Tablets)	95–120 per cent
Tabellæ Acidi Nicotinici	Nicotinic Acid Tablets (Niacin Tablets)	95–120 per cent
Tabellæ Atropinæ Sulfatis	Atropine Sulfate Tablets	93–107 per cent for tablets of 20 mg. or more. 90–110 per cent for tablets of less than 20 mg.
Tabellæ Barbitali	Barbital Tablets	94–106 per cent
Tabellæ Barbitali Sodici	Barbital Sodium Tablets (Soluble Barbital Tablets)	94–106 per cent
Tabellæ Cascaræ Sagradæ	Cascara Sagrada Tablets (Extract of Cascara Sagrada Tablets)	Prepared from extract of cascara sagrada. Tablets usually available contain 2, 3, or 5 grains of extract.
Tabellæ Chiniofoni	Chiniofon Tablets	Contain an amount of iodine (I) corresponding to 26.0–29.0 per cent of chiniofon.
Tabellæ Codeinæ Phosphatis	Codeine Phosphate Tablets	93–107 per cent
Tabellæ Codeinæ Sulfatis	Codeine Sulfate Tablets	93–107 per cent
Tabellæ Colchicinæ	Colchicine Tablets	90–110 per cent
Tabellæ Digitalis	Digitalis Tablets	Contain an amount of powdered digitalis corresponding in potency to 95–105 per cent of the labeled amount of powdered digitalis.
Tabellæ Dihydromorphinoni Hydrochloridi	Dihydromorphinone Hydrochloride Tablets	90–110 per cent
Tabellæ Ephedrinæ Sulfatis	Ephedrine Sulfate Tablets	93–107 per cent
Tabellæ Ergonovinæ Maleatis	Ergonovine Maleate Tablets	90–110 per cent
Tabellæ Ergotaminæ Tartratis	Ergotamine Tartrate Tablets	90–110 per cent
Tabellæ Erythritylis Tetranitratis	Erythrityl Tetranitrate Tablets (Erythritylis Tetranitras Dilutus U.S.P. XI, Erythrol Tetranitrate Tablets, Tetranitrol Tablets)	93–107 per cent
Tabellæ Extracti Fellis Bovis	Extract of Ox Bile Tablets	Contain an amount of the Extract corresponding, in their content of ox bile acids, determined as cholic acid, to not less than 40 per cent of the labeled amount of the Extract.
Tabellæ Ferri Sulfatis	Ferrous Sulfate Tablets	95–110 per cent
Tabellæ Glycerylis Trinitratis	Glyceryl Trinitrate Tablets (Nitroglycerin Tablets, Trinitrin Tablets)	80–112 per cent

Latin Title	*English Title and Synonym, if Any*	*Prescribed Limits of Labeled Amount of Active Ingredients Including All Tolerances*
Tabellæ Magnesii Phosphatis Tribasici	Tribasic Magnesium Phosphate Tablets	94–108 per cent
Tabellæ Magnesii Trisilicatis	Magnesium Trisilicate Tablets	Conform to the tests outlined in U.S.P. XII, pp. 472–473.
Tabellæ Menadioni	Menadione Tablets	95–115 per cent
Tabellæ Methenaminæ	Methenamine Tablets	95–105 per cent
Tabellæ Morphinæ Sulfatis	Morphine Sulfate Tablets	93–107 per cent
Tabellæ Neocinchopheni	Neocinchophen Tablets	94–106 per cent
Tabellæ Neostigminæ Bromidi	Neostigmine Bromide Tablets	93–107 per cent
Tabellæ Nicotinamidi	Nicotinamide Tablets (Niacinamide Tablets)	95–120 per cent
Tabellæ Pentobarbitali Sodici	Pentobarbital Sodium Tablets	90–105 per cent
Tabellæ Phenobarbitali	Phenobarbital Tablets	94–106 per cent
Tabellæ Phenobarbitali Sodici	Phenobarbital Sodium Tablets (Soluble Phenobarbital Tablets)	90–105 per cent
Tabellæ Potassii Chloridi	Potassium Chloride Tablets	95–105 per cent
Tabellæ Quinacrinæ Hydrochloridi	Quinacrine Hydrochloride Tablets	95–110 per cent
Tabellæ Quinidinæ Sulfatis	Quinidine Sulfate Tablets	94–106 per cent
Tabellæ Quininæ Sulfatis	Quinine Sulfate Tablets	94–106 per cent
Tabellæ Riboflavini	Riboflavin Tablets	95–120 per cent
Tabellæ Saccharini Sodici	Saccharin Sodium Tablets (Soluble Saccharin Tablets)	95–110 per cent
Tabellæ Sodii Nitritis	Sodium Nitrite Tablets	93–107 per cent
Tabellæ Sodii Salicylatis	Sodium Salicylate Tablets	93–107 per cent
Tabellæ Strychninæ Sulfatis	Strychnine Sulfate Tablets	93–107 per cent for tablets of 20 mg. or more. 90–110 per cent for tablets of less than 20 mg.
Tabellæ Sulfanilamidi	Sulfanilamide Tablets	95–105 per cent
Tabellæ Sulfapyridini	Sulfapyridine Tablets	95–105 per cent
Tabellæ Sulfathiazoli	Sulfathiazole Tablets	95–105 per cent
Tabellæ Theophyllinæ	Theophylline Tablets	94–106 per cent
Tabellæ Theophyllinæ Æthylenediaminicæ	Theophylline Ethylenediamine Tablets (Aminophylline Tablets)	Contain an amount of anhydrous theophylline corresponding to 73–84 per cent of labeled amount of theophylline ethylenediamine.
Tabellæ Theophyllinæ et Sodii Acetatis	Theophylline and Sodium Acetate Tablets	Contain an amount of anhydrous theophylline corresponding to 53–67 per cent of the labeled amount of theophylline and sodium acetate.
Tabellæ Thiaminæ Hydrochloridi	Thiamine Hydrochloride Tablets (Thiamin Chloride Tablets, Vitamin B_1 Tablets)	95–120 per cent
Tabellæ Thyroidei	Thyroid Tablets	Contain an amount of iodine (I) equivalent to 0.17–0.23 per cent of the labeled amount of thyroid.

TETRACAINÆ HYDROCHLORIDUM—Tetracaine Hydrochloride

(Tetracain. Hydrochlor.)

$C_{15}H_{24}N_2O_2.HCl$ Molecular weight, 300.82



Tetracaine Hydrochloride when dried over sulfuric acid for 18 hours contains not less than 86.5 per cent and not more than 88.5 per cent of tetracaine ($C_{15}H_{24}N_2O_2$).

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

Fine, white, crystalline powder; odorless; slightly bitter taste followed by a sense of numbness; very soluble in water; soluble in alcohol; insoluble in ether and in benzene; melts 147°–150° C.

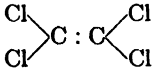
For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 494–495.

Remarks.—Also known as pantocaine. This is a local anesthetic similar to procaine which is said to be 15 times as active as novocaine and 10 times as active as cocaine but is more toxic. It is used in surface and spinal anesthesia. In the eye it is employed as a 0.5 per cent solution; in the nose and on other mucous membranes as a 2 per cent solution; and for spinal anesthesia a specially prepared 1 per cent solution is used.

TETRACHLOROÆTHYLENUM—Tetrachloroethylene

(Tetrachloroæthylen.—Perchloroethylene, Ethylene Tetrachloride)

C_2Cl_4 Molecular weight, 165.85



Tetrachloroethylene contains not less than 99 per cent and not more than 99.5 per cent of C_2Cl_4, the remainder consisting of alcohol.

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

Clear, colorless, mobile liquid; characteristic ethereal odor; non-inflammable; slowly decomposed by light and various metals in the presence of moisture; practically insoluble in water; miscible with an equal volume of alcohol, with ether, chloroform, petroleum benzin, and benzene; dissolves most of the fixed and volatile oils; specific gravity 1.600–1.620; boils 118°–122° C.

For *tests for purity* see U.S.P. XII, pp. 495–496.

Remarks.—Formerly official in N.F. VI. Also known as carbon dichloride. It was first prepared by Faraday in 1821 and is made by the action of chlorine on acetylene. It is an anthelmintic and is used in the removal of roundworm and hookworm. It is usually given in soft gelatin capsules, which are also official in U.S.P. XII, but has been administered to children on a lump of sugar.

Dose.—3 cc. (45 minims).

THEOBROMINA ET SODII ACETAS—Theobromine and Sodium Acetate

(Theobrom. et Sod. Acet.)

Theobromine and Sodium Acetate is a hydrated mixture of theobromine sodium ($C_7H_7N_4O_2Na$) and sodium acetate ($NaC_2H_3O_2$) in approximately molecular proportions. It yields not less than 55 per cent and not more than 65 per cent of theobromine ($C_7H_8N_4O_2$).

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White, crystalline powder; odorless or practically odorless; bitter taste; moderately hygroscopic and on exposure to air gradually absorbs carbon dioxide with the liberation of free theobromine; soluble in about 1.5 parts of water; slightly soluble in alcohol. Theobromine is precipitated from the aqueous solution even by adding weak acids.

For *identification, tests for purity* and *assay,* see U.S.P., pp. 496–497.

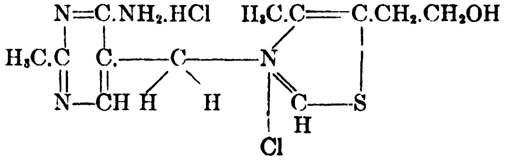
Remarks.—Also known as agurin. It is a diuretic and myocardial stimulant. It is claimed to be better tolerated by the stomach than theobromine sodium salicylate or theobromine itself and is more soluble than theobromine. It is inferior in diuretic power to theophylline but has greater power to sustain the diuresis produced. Capsules of this drug are also official in U.S.P. XII.

Dose.—0.5 Gm. (7½ grains).

THIAMINÆ HYDROCHLORIDUM—Thiamine Hydrochloride

(Thiamin. Hydrochlor.—Thiamin Chloride, Vitamin B1 Hydrochloride, Vitamin B1)

$C_{12}H_{17}ClN_4OS.HCl$ Molecular weight, 337.27



Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

Small, white crystals, or a crystalline powder; slight, characteristic odor; anhydrous product rapidly absorbs about 4 per cent of water when exposed to air; soluble in about 1 part of water and in about 100 parts of alcohol; soluble in glycerin; insoluble in ether and in benzene.

For *identification, tests for purity* and *assays for hydrogen chloride, nitrogen and sulfur,* see U.S.P. XII, pp. 500–501.

Remarks.—Also known as anti-beriberi or antineuritic vitamin, betabion, aneurine, betatoxin, oryzanin and torulin. First became official in Second Supplement to U.S.P. XI. Occurs in yeast, milk, rice husk, cereal grains, green leaves, roots and tubers. First isolated in crystalline form from rice polishings and is now manufacfactured synthetically. It is of value in correcting and preventing beriberi and certain cases of anorexia of dietary origin. It is said to have value in the treatment of alcoholic neuritis, neuritis of pregnancy and neuritis of pellagra. It has also been administered to secure optimal growth of infants and children and in the treatment of impaired lactation. Tablets of this drug are also official.

Dose.—5 mg. (1/12 grain).

TOTAQUINA—Totaquine

(Totaquin.)

Totaquine is a mixture of alkaloids from the bark of Cinchona succirubra Pavon and other suitable species of Cinchona. It contains not less than 7 per cent and not more than 12 per cent of anhydrous quinine, and a total of not less than 70 per cent and not more than 80 per cent of the anhydrous crystallizable cinchona alkaloids, the designation "crystallizable alkaloids" referring to cinchonidine, cinchonine, quinidine, and quinine.

Storage.—Preserve in well-closed, light-resistant containers.

Summarized Description.

Yellowish white to gray, or pale brown powder; odorless or nearly so; bitter taste; affected by light; almost insoluble in water; soluble in warm alcohol and in chloroform but usually there is some insoluble residue; partly soluble in ether.

For *identification, tests for purity* and *assays for quinine and cinchonidine, cinchonine, and quinidine,* see U.S.P. XII Sheet Supplement.

Remarks.—Intended as an economical substitute for quinine, as the mixed alkaloids of cinchona bark, even when relatively poor in quinine, are about as effective as quinine as an antimalarial. It was introduced at the request of the Philippine Government. The definition which appears above is not that to be found in U.S.P. XII but appears in the "Second U.S.P. XII Sheet Supplement." The standards appearing in U.S.P. XII were based on "Totaquine" made from cinchona barks from Java and the East Indies which are not now obtainable. The revised standards are based on "Totaquine" made from cinchona barks from Central and South America. Under regulations of the War Production Board, Totaquine can be sold only for antimalarial use.

Dose.—0.6 Gm. (10 grains).

TOXOIDUM TETANICUM—Tetanus Toxoid

(Tox. Tet.)

Tetanus Toxoid is a sterile solution of the products of growth of the tetanus bacillus (*Clostridium tetani*) so modified by special treatment as to have lost the ability to cause toxic effects in guinea pigs but retaining the property of inducing active immunity.

The toxicity of Tetanus Toxoid shall be so low that 5 cc. of the material does not cause any symptoms of tetanus in a guinea pig within a period of 21 days after its injection into the animal. The antigenic value shall be such that 1 cc. of the material 6 weeks after injection shall protect at least 80 per cent of guinea pigs from all symptoms of tetanus for a period of 10 days after the injection of 10 minimum lethal doses of tetanus test toxin into each animal.

Tetanus Toxoid complies with the requirements of the National Institute of Health of the United States Public Health Service.

Storage.—Preserve at a temperature of 2°–10° C., preferably at the lower limit; must be dispensed in manufacturer's original unopened glass container.

Summarized Description.

Clear, brownish yellow, or slightly turbid liquid; characteristic odor or odor due to preservative. For further *description* and *regulations affecting labeling,* see U.S.P. XII, p. 525.

A concentrated Tetanus Toxoid may be produced known as:

Tetanus Toxoid, Alum Precipitated—Refined Tetanus Toxoid

Summarized Description.

Turbid white or slightly gray suspension of alum precipitated Tetanus Toxoid in isotonic solution of sodium chloride. (For details, see U.S.P.) It meets the requirements as given under Tetanus Toxoid above with the exception of the requirement for antigenicity and in addition meets the following requirements:

The human dose of Tetanus Toxoid, Alum Precipitated, when administered subcutaneously to guinea pigs weighing 500 Gm., shall produce at least 2 units of antitoxin per cc. of blood serum in not more than 6 weeks. At least four guinea pigs shall be used for this test, but the blood serum from all of the test animals may be pooled for the test for antitoxin content.

The finished product shall contain not more than 20 mg. of alum per cc., the calculation being based on the total amount of alum added for precipitation.

Remarks.—Both forms are used for the production of active immunity against tetanus.

Dose.—Hypodermic, for active immunization, 1 cc., to be repeated at proper intervals.

TRIBROMOÆTHANOL—Tribromoethanol

(Tribromoæth.—Tribromoethyl Alcohol)

$C_2H_3Br_3O$ Molecular weight, 282.79

$Br_3C.CH_2OH$

Tribromoethanol, when dried over sulfuric acid for 18 hours, contains not less than 99 per cent of $C_2H_3Br_3O$.

Storage.—Preserve in tight, light-resistant containers.

Summarized Description.

White, crystalline powder; slight aromatic odor and taste; unstable in air or light; both aqueous and alcoholic solutions of this drug decompose on exposure to light; soluble in about 35 parts of water; very soluble in amylene hydrate; melts 79°–82° C.

For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 527.

Remarks.—Also known as ethobrom and avertin. It is used in solution in amylene hydrate for basal anesthesia by rectal administration. See Liquor Tribromoæthanolis, p. 26. It is also used in aqueous solution as a relaxant, before removing ureteral calculi, by instilling in the ureter. It has also been used in the control of convulsions in tetanus, in conjunction with tetanus antitoxin.

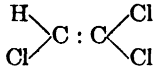
Dose.—Rectal (for each kilogram of body weight), 60 mg. (1 grain).

Caution.—The total amount administered should not exceed 8 Gm. for women or 10 Gm. for men, regardless of weight.

TRICHLOROÆTHYLENUM—Trichloroethylene

(Trichloroæthylen.)

C_2HCl_3 Molecular weight, 131.40



Trichloroethylene contains not less than 99 per cent and not more than 99.5 per cent of C_2HCl_3, the remainder consisting of alcohol.

Note.—Ammonium carbonate may be added as a preservative not in excess of 20 mg. per 100 cc.

Storage.—Preserve in sealed, light-resistant ampuls or frangible, light-resistant glass tubes. Prolonged exposure to excessive heat should be avoided. It must be dispensed in the manufacturer's original unopened glass container.

Summarized Description.

Clear, colorless, mobile liquid; characteristic odor resembling that of chloroform; slowly decomposed by light in the presence of moisture; noninflammable; practically insoluble in water; miscible with ether, alcohol, and chloroform; dissolves most fixed and volatile oils; specific gravity 1.456–1.462; boils 86°–88° C.

For *identification* and *tests for purity,* see U.S.P. XII, p. 528.

Remarks.—Also known as chlorylene and westrosol. Manufactured by boiling sym.-tetrachloroethane with lime. It is an analgesic which is said to be 13 times more active than chloroform and yet less toxic. It is administered by inhalation in trigeminal neuralgia and is also used in threatened attacks of angina pectoris.

Dose.—Inhalation, 1 cc. (15 minims).

UNGUENTUM ÆTHYLIS AMINOBENZOATIS—Ethyl Aminobenzoate Ointment

(Ung. Æthyl. Aminobenz.)

Condensed Recipe.

Incorporate 5 Gm. of Ethyl Aminobenzoate, in very fine powder, with 95 Gm. of White Ointment.

This monograph appears on p. 533 of U.S.P. XII.

Remarks.—Ethyl Aminobenzoate is also known as benzocaine and anæsthesin. The ointment is used in the treatment of minor burns and other skin conditions in which a mild local anesthetic action is desirable.

UNGUENTUM FLAVUM—Yellow Ointment

(Ung. Flav.)

Condensed Recipe.

Melt 5 Gm. of Yellow Wax in a suitable dish on a water bath, add 5 Gm. of Wool Fat and 90 Gm. of Petrolatum and continue heating until liquefied. Remove from heat and stir mixture until it congeals.

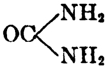
This monograph appears on p. 535 of U.S.P. XII.

Remarks.—This ointment is used as a base in the preparation of other ointments such as tannic acid ointment, belladonna ointment, phenol ointment and a number of other U.S.P. ointments in which the yellow color is not objectionable. In U.S.P. XI each of these ointment formulæ called for the ingredients of yellow ointment in variable proportions and the introduction of this base greatly simplifies the preparation of these ointments as it can be kept on hand already prepared.

UREA—Urea

(Carbamide)

CH_4N_2O Molecular weight, 60.06



$OC\begin{cases}NH_2\\NH_2\end{cases}$

Storage.—Preserve in well-closed containers.

Summarized Description.

Colorless to white, prismatic crystals or white, crystalline powder; almost odorless; cooling, saline taste; may gradually develop a slight odor of ammonia; soluble in 1.5 parts of water and in about 10 parts of alcohol; soluble in about 1 part of boiling alcohol; almost insoluble in chloroform and in ether; melts 131°–133° C.

For *identification* and *tests for purity,* see U.S.P. XII, pp. 541–542.

Remarks.—It is the diamide of carbonic acid and is also known as carbonyldiamine. It occurs in the urine of all mammals and also in the blood and tissue fluids. It is produced by the action of water on cyanamide. Urea is an active diuretic which is not poisonous and is rapidly eliminated. It has been used for the removal of necrotic tissue in infected wounds, for the removal of foul odors, and to promote healing. For external use it is used in urea pastes and in wet dressings or compresses. For further information, see Principles of Pharmacy, pp. 505, 755, 756 and 948.

Dose.—8 Gm. (2 drachms).

N.F. VII ADDITIONS

The following articles did not appear in either N.F. VI or U.S.P. XI but are official in N.F. VII.

CÆMENTUM ZINCI COMPOSITIONUM ET EUGENOLIS—Cement of Zinc Compounds and Eugenol

(Cæment. Zinc. et Eugenol.—Zinc-Eugenol Cement)

This preparation consists of a powder and a liquid, which are kept in separate containers until just before use, at which time a thick paste is prepared by mixing 10 parts of powder with 1 part of liquid. The amount of liquid may be varied to give any desired consistency.

Storage.—The powder is preserved in well-closed containers, and the liquid is preserved in tight containers, protected from light.

Condensed Recipe.

28.5 Gm. of rosin is powdered and mixed thoroughly with an equal weight of zinc oxide taken from 70.0 Gm. previously weighed. This mixture is sifted through a sieve of not less than 100 mesh and the residue remaining on the sieve is reground with more zinc oxide and sifted again, repeating the process until all of the material is passed through the sieve. 1.0 Gm. of zinc stearate and 0.5 Gm. of zinc acetate are thoroughly mixed with a portion of the zinc oxide and sifted through the 100 mesh sieve. The two powder mixtures and the rest of the zinc oxide are then thoroughly mixed. In the preparation of the liquid, 85.0 cc. of Eugenol is mixed with 15.0 cc. of cotton seed oil.

Summarized Description.

The powder is yellowish white to white in color. The liquid is thin, colorless to weak yellow; pungent spicy taste; strong aromatic odor of clove; specific gravity 1.043–1.048; refractive index 1.528–1.531 at 20° C.

For *identification of both liquid and powder* and for *assay for rosin* and *assay for zinc as zinc oxide,* see N.F. VII, pp. 67–68.

Remarks.—This is a preparation widely used in dentistry.

ELIXIR BENZALDEHYDI COMPOSITUM—Compound Elixir of Benzaldehyde

(Elix. Benzald. Comp.)

Storage.—Preserve in tight containers.

Alcohol Content.—From 3 to 5 per cent, by volume.

Condensed Recipe.

Ingredients.—Vanillin, 1.0 Gm.; benzaldehyde, 0.5 cc.; orange flower water, 150 cc.; alcohol, 50 cc.; syrup, 400 cc.; distilled water, enough to make 1000 cc.

Manipulation.—Dissolve the vanillin and benzaldehyde in the alcohol; add the syrup, the orange flower water, and the distilled water; mix and filter. For details, see N.F. VII, pp. 115–116.

Remarks.—This is a flavoring agent introduced to take the place of compound elixir of bitter almond which was official in N.F. VI and was not carried over into N.F. VII. It is an ingredient in Elixir of Three Bromides, N.F. VII.

FERRI OXIDUM FLAVUM—Yellow Ferric Oxide

(Ferr. Oxid. Flav.)

Yellow Ferric Oxide contains not less than 97.5 per cent of Fe_2O_3, calculated on the basis of the ignited product, the loss on ignition being determined on a separate sample.

Storage.—Preserve in well-closed containers.

Summarized Description.

Moderate yellowish orange powder, closely approximating the color of reference yellow ferric oxide; insoluble in water or in the organic solvents; nearly entirely soluble in hydrochloric acid upon warming.

For *tests for purity* and *assay,* see N.F. VII, p. 162.

Remarks.—Used as a coloring agent in the manufacture of Prepared Neocalamine N.F. VII.

FERRI OXIDUM RUBRUM—Red Ferric Oxide

(Ferr. Oxid. Rubr.)

Red Ferric Oxide contains not less than 90 per cent of Fe_2O_3 calculated on the basis of the ignited product, the loss on ignition being determined on a separate sample.

Storage.—Preserve in well-closed containers.

Summarized Description.

Moderate reddish brown powder closely approximating the color of a mixture of scarlet red 1 part, and red mercuric oxide 18 parts; insoluble in water or in the organic solvents; nearly entirely soluble in hydrochloric acid upon warming.

For *tests for purity* and *assay,* see N.F. VII, pp. 162–163.

Remarks.—Used as a coloring agent in the manufacture of Prepared Neocalamine N.F. VII. Red ferric oxides have also been named iron oxide red, iron sesquioxide, crocus martis adstringens, rubigo, ferrugo; venetian, stone or indian red.

LINIMENTUM NEOCALAMINÆ—Neocalamine Liniment

(Lin. Neocalam.)

Storage.—Preserve in tight containers.

Condensed Recipe.

Mix 150 Gm. of Prepared Neocalamine with 500 cc. of olive oil; to this gradually add with constant agitation 450 cc. of solution of calcium hydroxide; then add enough solution of calcium hydroxide to make 1000 cc. and mix well.

This liniment must be shaken thoroughly before dispensing.

The monograph for Neocalamine Liniment appears on p. 231 of N.F. VII.

Remarks.—See Neocalamina Præparata, p. 54.

LIQUOR ARGENTI NITRATIS AMMONIACALIS—Ammoniacal Solution of Silver Nitrate

(Liq. Arg. Nitrat. Ammon.—Ammoniacal Silver Nitrate, **Howe)**

Ammoniacal Solution of Silver Nitrate is an aqueous solution of silver diammino nitrate, containing in each 100 Gm. the equivalent of not less than 28.5 Gm. and not more than 30.5 Gm. of silver (Ag), and not less than 9.0 Gm. and not more than 9.7 Gm. of ammonia (NH_3).

Storage.—Preserve in small glass-stoppered containers, or in ampuls, and protect from light.

Condensed Recipe.

Powder 70.4 Gm. of silver nitrate in a glass mortar and dissolve it in 24.5 cc. of distilled water, warming if necessary. Cool to room temperature and add strong solution of ammonia from a burette until all but the last trace of black precipitate is dissolved. It will take about 68.0 cc. of the ammonia solution; the trace of precipitate remaining is filtered off.

Summarized Description.

Clear, colorless liquid; almost odorless; specific gravity about 1.48.

For *identification, tests for purity* and *assays for silver and ammonia,* see N.F. VII, pp. 240–241.

Remarks.—A preparation used extensively in dentistry. N.F. VII directs that for oral use the Ammoniacal Solution of Silver Nitrate should be mixed with a reducing agent, such as 10 per cent formaldehyde or eugenol, so as to deposit the metallic silver in the infected area in a state of fine subdivision.

LIQUOR MERBROMINI—Solution of Merbromin

(Liq. Merbrom.)

Solution of Merbromin yields from each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of anhydrous merbromin, not less than 0.43 Gm. and not more than 0.59 Gm. of Hg, and not less than 0.32 Gm. and not more than 0.47 Gm. of Br when assayed as directed.

Storage.—Preserve in tight containers.

Condensed Recipe.

Dissolve 20 Gm. of Merbromin in enough distilled water to make 1000 cc.

Description.—Clear, red liquid with a yellow-green fluorescence.

For *identification, tests for purity, assays for merbromin, bromine, and mercury,* see N.F. VII, p. 253.

Remarks.—See Merbrominum, p. 53. This aqueous solution is used as a general antiseptic on cuts and other wounds. It acts more slowly than tincture of iodine but its bacteriostatic effect lasts longer.

LIQUOR MERBROMINI CHIRURGICALIS—Surgical Solution of Merbromin

(Liq. Merbrom. Chir.)

Surgical Solution of Merbromin yields from each 100 cc., not less than 1.8 Gm. and not more than 2.2 Gm. of total solids, not less than 0.43 Gm. and not more than 0.59 Gm. of Hg, and not less than 0.32 Gm. and not more than 0.47 Gm. of Br when assayed as directed.

Storage.—Preserve in tight containers.

Condensed Recipe.

Dissolve 1 Gm. of monohydrated sodium carbonate in 350 cc. of distilled water, add 20 Gm. of merbromin and dissolve and then add 100 cc. of acetone and enough alcohol to make 1000 cc.

Description.—Clear, red liquid with a yellow-green fluorescence. For *identification, tests for purity* and *assays for total solids, bromine and mercury,* see N.F. VII, p. 254.

Remarks.—See Merbrominum, p. 53. This solution is more rapid in its action than Solution of Merbromin, which is an aqueous solution. Surgical Solution of Merbromin is used for disinfecting the skin before an operation.

LIQUOR PICIS CARBONIS CHLOROFORMICUS—Chloroformic Solution of Coal Tar

(Liq. Pic. Carbon. Chlorof.)

Storage.—Preserve in tight containers.

Condensed Recipe.

Mix 50 Gm. of coal tar with 800 cc. of chloroform, and shake until dissolved. Filter if necessary and add enough chloroform through the filter to make 1000 cc.

Description.—Yellowish brown in color; empyreumatic odor of coal tar associated with odor of chloroform.

This monograph appears on p. 257 of N.F. VII.

Remarks.—This is a new liquid preparation and is used where coal tar is indicated. The National Formulary monograph indicates that the product is for external use and is to be painted on the skin undiluted. Coal tar is a by-product in the destructive distillation of coal and solutions containing it are used in the treatment of pruritus, psoriasis, eczema and other skin diseases.

LIQUOR RESORCINOLIS FUSCI—Solution of Resorcin Brown

(Liq. Resorcin. Fusci)

Storage.—Preserve in tight containers.

Condensed Recipe.
Dissolve 0.5 Gm. of resorcin brown in enough distilled water to make 100 cc.

Summarized Description.
Clear, reddish brown liquid; odorless. For *identification,* see N.F. VII, p. 263.

Remarks.—See Resorcinol Fuscum, p 56.

LOTIO NEOCALAMINÆ—Neocalamine Lotion

(Lot. Neocalam.)

Storage.—Preserve in tight containers.

Condensed Recipe.
Dilute 400 cc. of magma of bentonite with an equal volume of water; thoroughly mix 150 Gm. of Prepared Neocalamine with about one-tenth of the diluted magma; gradually add the remainder of the diluted magma, add enough water to make 1000 cc. and shake well. The lotion must be shaken well before dispensing.
This monograph appears on p. 275 of N.F VII.

Remarks.—See Neocalamina Præparata, p. 54.

LOTIO NEOCALAMINÆ PHENOLATA—Phenolated Lotion of Neocalamine

(Lot. Neocalam. Phenol.—Compound Lotion of Neocalamine)

Storage.—Preserve in tight containers.

Condensed Recipe.
Mix 10 cc. of Liquefied Phenol with 990 cc. of Neocalamine Lotion. The lotion must be shaken well before dispensing.
This monograph appears on pp. 275–276 of N.F. VII.

Remarks.—See Neocalamina Præparata, p. 54.

MAGMA BENTONITI—Magma of Bentonite

(Magma Benton.)

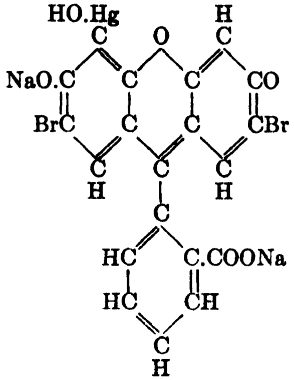
Storage.—Preserve in well-closed containers.

Condensed Recipe.
Sprinkle in small quantities 50 Gm. of bentonite upon 800 cc. of hot distilled water. All of the bentonite should be well wetted and the mixture is then allowed to stand, stirring occasionally for 24 hours; then stir until uniform throughout and add enough distilled water to make 1000 cc. and mix well.

Remarks.—Bentonite is a new item in U.S.P. XII (see p. 6). The magma is used in such products as Calamine Lotion and Neocalamine Lotion, both of which appear in N.F. VII, as a suspending agent.

MERBROMINUM—Merbromin

$C_{20}H_8O_6Br_2Na_2Hg$ Molecular weight, 750.70



Merbromin is the disodium salt of 2,7-dibrom-4-hydroxymercurifluorescein. When dried to constant weight at 110° C. and assayed as directed, Merbromin yields not less than 24 per cent and not more than 26.7 per cent of Hg, and not less than 18 per cent and not more than 21.3 per cent of Br.

Storage.—Preserve in tight containers.

Summarized Description.

Iridescent, green scales or granules; odorless; permanent in air; freely soluble in water; practically insoluble in alcohol and in acetone; insoluble in chloroform and in ether.

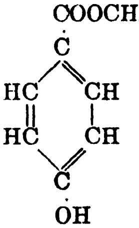
For *identification, tests for purity* and *assays for bromine and mercury,* see N.F. VII, pp. 285–286.

Remarks.—Both a solution of Merbromin and a surgical solution of Merbromin are official in N.F. VII. This product was first introduced under the trade name "Mercurochrome." Merbromin is a moderately active antiseptic and exerts bacteriostatic and bactericidal action when applied to the skin. It is used in cystitis and urethritis, in affections of the eye and of the ear, and in pyelitis.

METHYLIS PARAHYDROXYBENZOAS—Methyl Parahydroxybenzoate

(Meth. p-Hydroxybenz.)

$C_6H_4.OH.COOCH_3$ Molecular weight, 152.14



Methyl Parahydroxybenzoate, when dried to constant weight at 100° C., contains not less than 99 per cent of $C_6H_4.OH.COOCH_3$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Small, colorless crystals or white, crystalline powder; odorless or faint characteristic odor; slight burning taste; soluble in about 400 parts of water, in about 2.4 parts of alcohol and in about 8 parts of ether; soluble in 50 parts of water at 80° C.; slightly soluble in benzene and in carbon tetrachloride; melts 125°–127° C.

For *identification, tests for purity* and *assay,* see N.F. VII, pp. 286–287.

Remarks.—Also known as nipagin. It is used as a preservative in .05–.2 per cent concentrations in preparations for external use.

NEOCALAMINA PRÆPARATA—Prepared Neocalamine

(Neocalam. Præp.)

Prepared Neocalamine is zinc oxide admixed with not more than 7.5 per cent of ferric oxide, and contains, after ignition, not less than 92 per cent of ZnO (81.38).

Storage.—Preserve in well-closed containers.

Condensed Recipe.

Mix thoroughly together 3.0 Gm. of red ferric oxide, 4.0 Gm. of yellow ferric oxide, and 93.0 Gm. of zinc oxide.

Summarized Description.

Fine powder; weak yellowish orange color; odorless; almost tasteless; insoluble in water and in alcohol; soluble almost completely in mineral acids.

For *identification, tests for purity* and *assay,* see N.F. VII, pp. 295–296.

Remarks.—This is a specially prepared calamine which more nearly duplicates the color of flesh. A lotion, a phenolated lotion, an ointment and a liniment are official in N.F. VII. These products are used as a protective in eczema and other skin diseases.

PASTA PECTINI—Pectin Paste

(Past. Pectin.)

Storage.—Preserve in tight containers and avoid excessive heat. After a few months it may deteriorate and show some liquefaction.

Condensed Recipe.

Dissolve 2 Gm. of benzoic acid in 825 cc. of isotonic solution of three chlorides heated to 100° C.; mix 75 Gm. of pectin and 180 Gm. of glycerin in a large dry vessel until all of the particles of pectin are covered. While stirring add all of the hot benzoic acid solution, and continue stirring until a homogeneous paste is formed. (Makes about 1000 Gm.)

This monograph appears on p. 312 of N. F. VII.

Remarks.—See Pectin, below.

PASTA PECTINI TENUIS—Thin Pectin Paste

(Past. Pectin. Ten.)

Storage.—Preserve in tight containers and avoid excessive heat. After a few months it may deteriorate and show some liquefaction.

Condensed Recipe.

Dissolve 2 Gm. of benzoic acid in 950 cc. of isotonic solution of three chlorides heated to 100° C. Mix 35 Gm. of pectin with 70 Gm. of glycerin in a large dry vessel until all of the pectin is coated with glycerin. While stirring, add benzoic acid solution and continue to stir until a homogeneous paste is formed.

This monograph appears on p. 313 of N.F. VII.

Remarks.—See Pectum, below.

PECTINUM—Pectin

Pectin is a purified carbohydrate product obtained from the dilute acid extract of the inner portion of the rind of citrus fruits, or from apple pomace. It consists chiefly of partially methoxylated polygalacturonic acids.

Pectin yields not less than 7 per cent of methoxyl groups and not less than 78 per cent of galacturonic acid based on a total ash and moisture-free basis. It also yields not more than 4 per cent of total ash, not more than 0.4 per cent of acid-insoluble ash, and not more than 10 per cent of moisture.

Note.—Commercial pectin for the production of jellied food products is standardized to the convenient "100 jelly grade" by addition of dextrose or other sugars and sometimes contains sodium citrate or other buffer salts. This monograph refers to the pure pectin to which no such additions have been made.

Storage.—Preserve in tight containers.

Summarized Description.

Yellowish white coarse or fine powder; almost odorless; mucilaginous taste; almost completely soluble in 20 parts of water forming a viscous opalescent colloidal solution which flows readily and is acid to litmus paper; insoluble in alcohol or diluted alcohol; insoluble in other organic solvents; dissolves more readily in water if first moistened with alcohol, glycerin, or simple syrup, or if first mixed with 3 or more parts of sucrose.

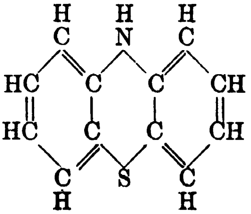
For *identification, tests for purity* and *assays for methoxyl groups and galacturonic acid,* see N.F. VII, pp. 317–318.

Remarks.—Pectin pastes were originally developed by Dr. Bernard Fantus for the treatment of bed sores and indolent ulcers. Two such pastes are official in N.F. VII, Pectin Paste and Thin Pectin Paste.

PHENOTHIAZINA—Phenothiazine

(Phenothiaz.—Thiodiphenylamine)

$C_{12}H_9NS$ Molecular weight, 199.26



Phenothiazine, when dried to constant weight at 100° C., contains not less than 95 per cent of $C_{12}H_9NS$.

Storage.—Preserve in well-closed containers.

Summarized Description.

Weak yellow-green to weak olive-green powder; tasteless; slight characteristic odor; slowly oxidized when exposed to the air over a long period of time (color darkens); soluble in about 75 parts of alcohol, in about 5 parts of acetone, and in about 45 parts of toluene; usually incompletely soluble in ether; insoluble in water; melts 181°–185° C.

For *identification, tests for purity* and *assay,* see N.F. VII, pp. 322–323.

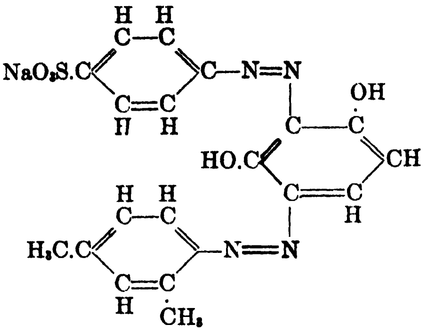
Remarks.—Prepared by fusing diphenylamine with sulfur in the presence of iodine as a catalyst. Has been used as a spray or dust insecticide to replace lead arsenate in eliminating the codling moth but introduced into N.F. VII as an anthelmintic for veterinary use.

Dose.—For dosage in the treatment of various animals see N.F. VII. The National Formulary monograph cautions that animals should be treated with Phenothiazine only under the advice of a veterinarian.

RESORCINOL FUSCUM—Resorcin Brown

(Resorc. Fuscum—D & C Brown No. 1)

$C_{20}H_{17}N_4O_5SNa$ Molecular weight, 448.43



Resorcin Brown is the monosodium salt of 4-*p*-sulfophenylazo-2-(2,4-xylylazo)-1,3-resorcinol.

Storage.—Preserve in well-closed containers, protected from light.

Summarized Description.

Strong brown to deep brown powder; soluble in about 15 parts of water; soluble in glycerin, methyl and ethyl alcohol; sparingly soluble in ethyl ether and in acetone.

For further information see N.F. VII, p. 359.

Remarks.—This is a permitted coloring agent for drugs and cosmetics under the Federal Food, Drug and Cosmetic Act. An aqueous solution of this color is also official in N.F. VII and is used to color Solution of Nux Vomica Alkaloids N.F. VII.

SPIRITUS BENZALDEHYDI—Spirit of Benzaldehyde

(Sp. Benzald.)

Storage.—Preserve in tight containers, protected from light.

Alcohol Content.—From 71 to 78 per cent, by volume.

Condensed Recipe.

Dissolve 10 cc. of Benzaldehyde in 800 cc. of alcohol, and add enough distilled water to make 1000 cc.

This monograph appears on p. 384 of N.F. VII.

Remarks.—Introduced into N.F. VII to replace spirit of bitter almond. It is used as a flavoring agent.

Dose.—0.5 cc. (8 minims). This dose contains 0.005 cc. of Benzaldehyde.

SUCCUS CERASI—Cherry Juice

(Suc. Cer.)

Cherry Juice is the liquid expressed from the fresh ripe fruit of *Prunus Cerasus* Linné (Fam. *Rosaceæ*).

Cherry Juice contains not less than 1.0 per cent of malic acid.

Storage.—Preserve in tight containers, protected from sunlight; avoid excessive heat.

Condensed Preparation.

Coarsely crushed sour cherries, including the broken pits and with 0.1 per cent of benzoic acid dissolved in the mixture, are allowed to stand for a period of time after which the juice is pressed from the mixture and filtered. For details, see N.F. VII.

Summarized Description.

Clear liquid which is red to reddish orange in color when freshly prepared; aromatic, characteristic odor; sour taste; specific gravity 1.045–1.075; refractive index not less than 1.3500.

For *tests for purity* and *assay,* see N.F. VII, pp. 393–394.

Remarks.—Cherry Juice is an ingredient of Syrup of Cherry which in N.F. VI was made directly from the sour cherries. Syrup of Cherry is a flavoring agent and is an ingredient of Syrup of Ephedrine Sulfate N.F. VII.

SUCCUS RUBI IDÆI—Raspberry Juice

(Suc. Rub. Id.)

Raspberry Juice is the liquid expressed from the fresh ripe fruit of varieties of *Rubus idæus* Linné or of *Rubus strigosus* Michaux (Fam. *Rosaceæ*).

Raspberry Juice contains not less than 1.5 per cent of citric acid.

Storage.—Preserve in tight containers, protected from sunlight; avoid excessive heat.

Condensed Recipe.

The juice expressed from fresh, ripe raspberries, and with 0 1 per cent of benzoic acid dissolved in it, is allowed to stand for a period of time and is then filtered. For details, see N.F. VII.

Summarized Description.

Clear liquid; aromatic, characteristic odor; characteristic, sour taste; red to reddish orange color when freshly prepared; specific gravity 1.025–1.045; refractive index not less than 1.3445.

For *identification, tests for purity* and *assay,* see N.F. VII, pp. 394–396.

Remarks.—Raspberry Juice is an ingredient of Syrup of Raspberry which in N.F. VI was made directly from fully ripe raspberries. Syrup of Raspberry is a flavoring agent and is an ingredient of Elixir of Five Bromides N.F. VII and of Glycerinated Elixir of Gentian N.F. VII.

SYRUPUS PINI ALBÆ COMPOSITUS CUM CODEINA—Compound Syrup of White Pine with Codeine

(Syr. Pin. Alb. Comp. c. Codein.)

Storage.—Preserve in tight containers; avoid excessive heat.

Alcohol Content.—From 10 to 12 per cent, by volume.

Condensed Recipe.

Dissolve 2 Gm. of Codeine Phosphate in 10 cc. of Distilled Water using heat and mix this solution with enough Compound Syrup of White Pine to make 1000 cc.

This monograph appears on p. 410 of N.F. VII.

Remarks.—This preparation replaces Compound Syrup of White Pine with Morphine which was official in N.F. VI. The amount of Codeine Phosphate has been adjusted so as to correspond to the difference in potency of the alkaloidal salts. This is a cough syrup.

Dose.—4 cc. (1 fluidrachm). This dose contains 8 mg. of Codeine Phosphate.

UNGUENTUM NEOCALAMINÆ—Ointment of Neocalamine

(Ung. Neocalam.)

Storage.—Preserve in tight containers; avoid prolonged exposure to temperatures above 30° C.

Condensed Recipe.

Mix 37.5 Gm. of petrolatum and 12.5 Gm. of wool fat; incorporate 25.0 cc. of water in small quantities until all is emulsified; triturate until well mixed 15.0 Gm. of Prepared Neocalamine with 10.0 cc. of liquid petrolatum and mix this paste with the cream until a smooth product is formed.

This monograph appears on p. 473 of N.F. VII.

Remarks.—See Prepared Neocalamine, p. 54.

CHANGES AND CORRECTIONS IN "PRINCIPLES OF PHARMACY" TO CONFORM WITH CHANGES AND CORRECTIONS IN THE U.S.P. XII AND N.F. VII

Based on the U.S.P. XII and N.F. VII and Supplements issued up to January, 1943.

The corrections and changes are listed alphabetically according to the official Latin title of the drug or preparation unless otherwise specified. The page number or numbers, unless otherwise specified, refer to the page or pages in the Fourth Edition of "Principles of Pharmacy." Students and others using "Principles of Pharmacy" will find it to their advantage to mark the text pages of the book, in accordance with this Supplement, to indicate where changes or modifications in the text are necessary to make it conform to the corrections and additions to the U.S.P. XII and N.F. VII.

ARTICLES OFFICIAL IN THE U.S.P. XI BUT NOT ADMITTED TO THE U.S.P. XII AND *NOT ADDED* TO THE N.F. VII

	Page in Principles of Pharmacy
Acidum Acetyltannicum	810
Acidum Sulfuricum Aromaticum	450
Albumini Tannas	950
Ammonii Benzoas	504
Calcii Bromidum	523
Cannabis	858
Emulsum Asafœtidæ	286
Extractum Cannabis	299
Fluidextractum Cannabis	264
Galla	812
Magma Ferri Hydroxidi	572
Merbaphenum	786
Oleum Maydis	731
Terebenum	828
Unguentum Gallæ	366

ARTICLES OFFICIAL IN THE U.S.P. XI BUT NOT ADMITTED TO THE U.S.P. XII AND *ADDED* TO THE N.F. VII

	Page in Principles of Pharmacy
Acetum Scillæ	277
Acidum Aceticum Dilutum	670
Aconitum	934
Acriflavina	781
Acriflavinæ Hydrochloridum	781
Æthylhydrocupreinæ Hydrochloridum	915
Ammonii Bromidum	504
Ammonii Salicylas	508
Arseni Triiodidum	583
Asafœtida	876
Bismuthi Subgallas	602
Calcii Creosotas	793
Cantharis	959
Capsicum	859
Carbromalum	759
Ceratum Cantharidis	361
Cinchona	936
Copaiba	865
Creosoti Carbonas	792
Creosotum	791
Dichloramina-T	806
Elixir Glycyrrhizæ	227
Emplastrum Cantharidis	377
Extractum Nucis Vomicæ	302
Ferrum	556
Fluidextractum Belladonnæ Radicis	264
Guaiacol	776
Hydrargyri Iodidum Flavum	619
Iodoformum	647
Kino	812
Liquor Ammonii Acetatis	209
Liquor Ferri Chloridi	566
Liquor Ferri Tersulfatis	568
Liquor Sodii Hypochloritis Dilutus	424
Massa Hydrargyri	612
Mistura Opii et Glycyrrhizæ Composita	279
Oleum Santali	843
Paraffinum	644
Paraffinum Chlorinatum	644
Pepsinum	954
Pilulæ Aloes	340
Podophyllum	879
Potassii Chloras	467
Pulvis Ipecacuanhæ et Opii	316
Pulvis Sennæ Compositus	316
Pyrogallol	778
Quinina	916
Resina Podophylli	305

	Page in Principles of Pharmacy
Santoninum	878
Scilla	718
Serpentaria	857
Sodii Acetas	480
Spiritus Æthylis Nitritis	662
Spiritus Chloroformi	204
Strychninæ Nitras	922
Sulfonethylmethanum	676
Sulfur Lotum	429
Syrupus Ferri Iodidi	562
Syrupus Scillæ	221
Theobromina cum Sodii Salicylate	762

	Page in Principles of Pharmacy
Tinctura Aconiti	243
Tinctura Cantharidis	245
Tinctura Capsici	246
Tinctura Cinchonæ Composita	246
Tinctura Ferri Chloridi	566
Tinctura Kino	249
Tinctura Scillæ	251
Tinctura Valerianæ	252
Tinctura Veratri Viridis	252
Valeriana	844
Veratrum Viride	935

ARTICLES OFFICIAL IN N.F. VI BUT NOT INCLUDED IN N.F. VII

Æthylis Carbamas
Amaranthum
Ampullæ Bismuthi Subsalicylatis
Ampullæ Caffeinæ cum Sodii Benzoate
Ampullæ Calcii Gluconatis
Ampullæ Dextrosi
Ampullæ Dextrosi et Sodii Chloridi
Ampullæ Emetinæ Hydrochloridi
Ampullæ Epinephrinæ Hydrochloridi
Ampullæ Hydrargyri Salicylatis
Ampullæ Pituitarii Posterioris
Ampullæ Quininæ Hydrochloridi et Æthylis Carbamatis
Ampullæ Sodii Chloridi
Ampullæ Sodii Citratis
Aqua
Calcii Phosphas Præcipitatus
Cascara Amarga
Curatio Paraffini
Elixir Amygdalæ Compositum
Elixir Aquosum
Elixir Chloralis et Potassii Bromidi Compositum
Elixir Phenobarbitali
Fluidextractum Trifolii Compositum
Liquor Amaranthi
Liquor Dextrosi et Sodii Chloridi Isotonicus
Methylrosanilinum
Potassii Chloridum
Prunus Cerasus
Quininæ Hydrochloridum
Rubus Idæus
Spiritus Amygdalæ Amaræ
Syrupus Glycyrrhizæ
Syrupus Pini Albæ Compositus cum Morphina
Syrupus Trifolii Compositus
Tabellæ Acetophenetidini
Tabellæ Acidi Acetylsalicylici
Tabellæ Atropinæ Sulfatis
Tabellæ Barbitali
Tabellæ Barbitali Solubilis
Tabellæ Codeinæ Phosphatis
Tabellæ Codeinæ Sulfatis
Tabellæ Methenaminæ
Tabellæ Morphinæ Sulfatis
Tabellæ Phenobarbitali
Tabellæ Phenobarbitali Solubilis
Tabellæ Quininæ Sulfatis
Tabellæ Sodii Nitritis
Tabellæ Sodii Salicylatis
Tabellæ Strychninæ Sulfatis
Tetrachloroethylenum
Tinctura Gallæ

Of the above 51 articles appearing in N.F. VI but not appearing in N.F. VII, all but 12 now appear in identical or similar form in U.S.P. XII. Of these 12 articles not appearing in either N.F. VII or U.S.P. XII, there are several for which new monographs of similar products appear in N.F. VII such as Compound Syrup of White Pine with Codeine replacing Compound Syrup of White Pine with Morphine, Spirit of Benzaldehyde replacing Spirit of Bitter Almond and others. Following is the list of the 12 articles dropped because they apparently no longer enjoy an extent of use which justifies their inclusion in N.F. VII.

Cascara Amarga
Curatio Paraffini
Elixir Amygdalæ Compositum
Elixir Aquosum
Elixir Chloralis et Potassii Bromidi Compositum
Fluidextractum Trifolii Compositum
Prunus Cerasus
Rubus Idæus
Spiritus Amygdalæ Amaræ
Syrupus Pini Albæ Compositus cum Morphina
Syrupus Trifolii Compositus
Tinctura Gallæ

CHANGES IN TITLES IN U.S.P. XII

Changes in Official Latin Titles

U.S.P. XI	U.S.P. XII
Aqua Ammoniæ	Liquor Ammoniæ Dilutus
Aqua Ammoniæ Fortior	Liquor Ammoniæ Fortis
Barbitalum Solubile	Barbitalum Sodicum
Caffeina cum Sodii Benzoate	Caffeina et Sodii Benzoas
Erythritylis Tetranitras Dilutus	Tabellæ Erythritylis Tetranitratis
Fluoresceinum Solubile	Fluoresceinum Sodicum
Glucosum	Glucosum Liquidum
Iodophthaleinum Solubile	Iodophthaleinum Sodicum
Liquor Acidi Arsenosi	Liquor Acidi Arseniosi
*Liquor Epinephrinæ Hydrochloridi	Liquor Epinephrinæ Hydrochloridi Injectio Epinephrinæ Hydrochloridi
Liquor Hepatis Purificatus	Injectio Hepatis
Liquor Histaminæ Phosphatis	Injectio Histaminæ Phosphatis
Liquor Iodi Compositus	Liquor Iodi Fortis
Liquor Parathyroidei	Injectio Parathyroidei
Liquor Pituitarii Posterioris	Injectio Pituitarii Posterioris
Liquor Sodii Chloridi Physiologicus	Liquor Sodii Chloridi Isotonicus
Nitrogenii Monoxidum	Oxidum Nitrosum
Oleum Sinapis Volatile	Allylis Isothiocyanas
Pentobarbitalum Solubile	Pentobarbitalum Sodicum
Phenobarbitalum Solubile	Phenobarbitalum Sodicum
Pulvis Chiniofoni	Chiniofonum
Saccharinum Solubile	Saccharinum Sodicum
Sapo Mollis	Sapo Mollis Medicinalis
Stomachus	Stomachus Pulveratus
Theophyllina cum Æthylenediamina	Theophyllina Æthylenediaminica
Theophyllina cum Sodii Acetate	Theophyllina et Sodii Acetas
Toxinum Diphthericum Detoxicatum	Toxoidum Diphthericum
Unguentum	Unguentum Album

Changes in Official English Titles

U.S.P. XI	U.S.P. XII
Ammonia Water	Diluted Solution of Ammonia
Antipneumococcic Serum	Antipneumococcic Serum—Type Specific
Caffeine with Sodium Benzoate	Caffeine and Sodium Benzoate
Chiniofon Powder	Chiniofon
Compound Solution of Iodine	Strong Solution of Iodine
Diluted Erythrityl Tetranitrate	Erythrityl Tetranitrate Tablets
Glucose	Liquid Glucose
Nitrogen Monoxide	Nitrous Oxide
Ointment	White Ointment
Physiological Solution of Sodium Chloride	Isotonic Solution of Sodium Chloride
Purified Petroleum Benzin	Purified Benzin
Purified Solution of Liver	Liver Injection
Soft Soap	Medicinal Soft Soap
Soluble Barbital	Barbital Sodium
Soluble Fluorescein	Fluorescein Sodium
Soluble Iodophthalein	Iodophthalein Sodium
Soluble Pentobarbital	Pentobarbital Sodium
Soluble Phenobarbital	Phenobarbital Sodium
Soluble Saccharin	Saccharin Sodium
Solution of Arsenous Acid	Solution of Arsenious Acid

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* Liquor Epinephrinæ Hydrochloridi was formerly used for oral as well as for intravenous purposes. A non-sterile solution under this title is now retained for oral use, while a sterile solution is recognized under the title Injectio Epinephrinæ Hydrochloridi.

Changes in Official English Titles

U.S.P. XI	U.S.P. XII
*Solution of Epinephrine Hydrochloride	Solution of Epinephrine Hydrochloride Epinephrine Hydrochloride Injection
Solution of Histamine Phosphate	Histamine Phosphate Injection
Solution of Liver	Liver Injection
Solution of Parathyroid	Parathyroid Injection
Solution of Posterior Pituitary	Posterior Pituitary Injection
Stomach	Powdered Stomach
Stronger Ammonia Water	Stronger Solution of Ammonia
Theophylline with Ethylene Diamine	Theophylline Ethylenediamine
Theophylline with Sodium Acetate	Theophylline and Sodium Acetate
Volatile Oil of Mustard	Allyl Isothiocyanate

CHANGES IN TITLES IN NATIONAL FORMULARY VII

Changes in Latin Titles

N.F. VI	N.F. VII
Cacao Præparatum	Cacao
Chlorthymol	Chlorothymol
Collodium Salicylicum Compositum	Collodium Salicylicum
Convallariæ Radix	Convallaria
Elixir Sabal et Santali Compositum	Elixir Serenoæ et Santali Compositum
Fluidextractum Convallariæ Radicis	Fluidextractum Convallariæ
Fluidextractum Sabal	Fluidextractum Serenoæ
Liquor Methylrosanilini	Liquor Methylrosanilini Chloridi
Mistura Rhei Composita	Mistura Rhei et Sodæ
Ovi Vitellus Recens	Ovi Vitellus
Pilulæ Rhei Compositæ	Pilulæ Rhei et Aloes
Sabal	Serenoa
Syrupus Cacao Præparati	Syrupus Cacao
Tinctura Rhei Composita	Tinctura Rhei
Unguentum Acidi Benzoici Compositum	Unguentum Acidi Benzoici et Salicylici

Changes in English Titles

N.F. VI	N.F. VII
Chlorthymol	Chlorothymol
Compound Elixir of Sabal and Sandalwood	Compound Elixir of Serenoa and Sandalwood
Compound Mixture of Rhubarb	Mixture of Rhubarb and Soda
Compound Ointment of Benzoic Acid	Ointment of Benzoic and Salicylic Acid
Compound Pills of Rhubarb	Pills of Rhubarb and Aloe
Compound Salicylic Collodion	Salicylic Collodion
Compound Tincture of Rhubarb	Tincture of Rhubarb
Convallaria Root	Convallaria
Fluidextract of Convallaria Root	Fluidextract of Convallaria
Fluidextract of Sabal	Fluidextract of Serenoa
Fresh Egg Yolk	Egg Yolk
Prepared Cacao	Cacao
Sabal	Serenoa
Solution of Methyl-rosaniline	Solution of Methylrosaniline Chloride
Syrup of Prepared Cacao	Syrup of Cacao

*** Solution of Epinephrine Hydrochloride was formerly used for oral as well as for intravenous purposes. A non-sterile solution under this title is now retained for oral use, while a sterile solution is recognized under the title Epinephrine Hydrochloride Injection.**

CHANGES IN MONOGRAPHS OF U.S.P. AND N.F.

Acidum Aceticum—Page 669: Change Storage to "Preserve in glass bottles having closures which are not affected by the acid." For *identification, tests for purity* and *assay,* see U.S.P. XII, p. 12.

Acidum Aceticum Glaciale—Page 668: In first line, change "99" to "99.4." Change "Storage" to "Preserve in glass bottles having closures which are not affected by the Acid." Change U.S.P. page references to "U.S.P. XII, p. 13."

Acidum Acetylsalicylicum—Page 803: Change molecular weight to 180.15. In first line change "to constant weight over sulfuric acid" to "over sulfuric acid for 5 hours." For revised *description, identification, tests for purity* and *assay,* see U.S.P. XII, pp. 13–14.

Acidum Citricum—Page 688: In first line, change "99.5" to "99.7."

Acidum Hydrochloricum—Page 443: In second line, change "37" to "38" and in sixth line, change "1.175" to "1.18." Change "Storage" to "Preserve in tight containers."

Acidum Hydrochloricum Dilutum—Page 444: Change "Storage" to "Preserve in tight containers." Change "Dose" to "4 cc. (1 fluidrachm)."

Acidum Nitricum—Page 445: In first line, change "70" to "71" and in seventh line, change "1.403" to "1.41." Change "Storage" to "Preserve in tight containers." Change U.S.P. page references to "U.S.P. XII, p. 26."

Acidum Salicylicum—Page 799: In first line, change "dried at 100° C. for two hours" to "when dried over sulfuric acid for 5 hours." Change "Storage" to "Preserve in well-closed containers." In seventh line, on page 800, change "157° and 159°" to "158° and 160°." Change U.S.P. page references to "U S.P. XII, pp. 28–29."

Acidum Tannicum—Page 809: Change first line to "A tannin usually obtained from nutgalls, the excrescences obtained from the young twigs of *Quercus infectoria* Olivier, and other allied species of *Quercus* (Fam *Fagaceæ*) The dose has been deleted from U S.P. XII. Change U.S.P. page references to "U.S.P. XII, pp. 31–32."

Acidum Tartaricum—Page 685: Change rubric to "Tartaric Acid, when dried over sulfuric acid for 5 hours, contains not less than 99.7 per cent of $H_2C_4H_4O_6$." Change Solubilities to "soluble in about 0.8 parts of water, in about 3 parts of alcohol and in 5 parts of boiling water." Change U S.P. page references to "U.S.P. XII, p. 32."

Aconitum—Page 934: Substitute the following definition from N.F. VII: Aconite is the dried tuberous root of *Aconitum Napellus* Linné (Fam. *Ranunculaceæ*). The potency of Aconite shall be such that 0.1 Gm. of it, when extracted and the extract assayed as directed under *Tinctura Aconiti* (page 441, N.F. VII), shall possess an activity equivalent to not less than 0.150 mg. of reference aconitine. Aconite contains not more than 5 per cent of its stems and not more than 2 per cent of other foreign organic matter. For *description, histology* and *assays,* see N.F. VII, p. 17.

Æthylis Chaulmoogras—Page 736: Change "Dose" to "Oral or intramuscular, 2 cc. (30 minims)." Change U.S.P. page references to "U.S.P. XII, pp. 40–41."

Agar—Page 707: In the second line, on page 708, change "18" to "20." Change "Dose" to "4 Gm. (1 drachm)." See U.S.P. XII, p. 43.

Aloe—Page 895: Substitute the following definition from U.S.P. XII: Aloe is the dried juice of the leaves of *Aloe Perryi* Baker, known in commerce as Socotrine Aloe, or of *Aloe barbadensis* Miller (*Aloe vera* "Linné"), known in commerce as Curaçao Aloe, or of *Aloe ferox* Miller and hybrids of this species with *Aloe africana* Miller and *Aloe spicata* Baker, known in commerce as Cape Aloe (Fam. *Liliaceæ*). Aloe yields not less than 50 per cent of water-soluble extractive, p. 632, U.S.P. XII. It contains not more than 12 per cent of moisture when determined by the "Toluene Method—IX," p. 629, U.S.P. XII, and yields not more than 4 per cent of ash, p. 628, U.S.P. XII. For *description, identification, test for alcohol-insoluble matter* and *assay,* see U.S.P. XII, pp. 46–47.

Alumen—Page 546: Correct solubilities as follows: Ammonium Alum soluble in 7 parts of water, and in about 0.3 parts of boiling water; Potassium Alum soluble in 7.5 parts of water, and in about 0.3 parts of boiling water. Alum is insoluble in alcohol and is freely but slowly soluble in glycerin. Correct molecular weight of Potassium Alum to 474.38. For *description, tests for purity* and *assay*, see U.S.P. XII, p. 49.

Ammonii Carbonas—Page 505: In the third line, change "32" to "33." See U.S.P. XII, pp. 52–53.

Ammonii Chloridum—Page 507: In first line, change "twenty-four hours" to "four hours." Under "Summarized Description," change "white, granular powder" to "colorless crystals or white, fine or coarse, crystalline powder." In second line, change "82" to "100" and "10" to "8." Change "Dose" to "Expectorant, single dose 0.3 Gm. (5 grains); diuretic, daily dose 3 to 6 Gm. (45 to 90 grains)." Change U.S.P. page references to "U.S.P. XII, p. 53."

Ampuls—Pages 988–991: For latest information see "Ampullæ," N.F. VII, pp. 29–38 and "Injectiones" in this supplement.

Antitoxinum Diphthericum—Page 978: In second line, delete "of the genus *Equus*" and add at end of paragraph: "Diphtheria Antitoxin complies with the requirements of the National Institute of Health of the United States Public Health Service." Change "Dose" to "Parenteral, therapeutic, 20,000 units; prophylactic, 1000 units." For further details and regulations, see U.S.P. XII, pp. 57–58.

Antitoxinum Scarlatinæ Streptococcicum—Page 979: Official English title is now "Scarlet Fever Streptococcus Antitoxin." In second line, delete "of the genus *Equus*" and in third line, delete "or toxin-like substance." The second and third sentences of the first paragraph do not appear in U.S.P. XII. Add to first paragraph: "Scarlet Fever Streptococcus Antitoxin complies with the requirements of the National Institute of Health of the United States Public Health Service." For further details and regulations, see U.S.P. XII, pp. 58–59.

Antitoxinum Tetanicum—Page 979: In second sentence delete wording "of the genus *Equus*." In the third line on page 980 change the figure "300" to "400" and add to this paragraph the sentence, "Tetanus Antitoxin complies with the requirements of the National Institute of Health of the United States Public Health Service." For *description* and *regulations*, see U.S.P. XII, pp. 59–60.

Apii Fructus—Celery Fruit (Celeryseed): This is not mentioned in "Principles of Pharmacy." It is official in N.F. VII and is the dried ripe fruit of *Apium graveolens* Linné (Fam. *Umbelliferæ*). Each 100 Gm. of the drug yields not less than 1.75 cc. of a volatile oil which contains d-limone. Celeryseed is given as a stimulant in doses of 2 Gm. (30 grains); also used as a condiment.

Apocynum—Page 880: The synonyms "Black Indian Hemp" and "Canada-hemp" have been added in the N.F. VII monograph The average dose is given as 60 mg (1 grain).

Aqua Aurantii Florum—Page 198: The First Supplement to N.F. VII permits until further notice the use of Water in place of Orange Flower Water in N.F. preparations in which it is an ingredient.

Aqua Destillata Sterilisata—Page 414: Change monograph to read as follows: "*Caution—Sterilized Distilled Water and Distilled Water are not to be used for parenteral administration or in preparations to be used parenterally. For such purpose, Water for Injection*" (U.S.P. XII, page 66 and in this supplement) "*is to be used.* Place distilled water in sterilized, suitable containers, properly sealed or closed, and sterilize preferably by Process C. See *Sterilization Methods*, U.S.P. XII, page 169. *Storage*—Preserve in the container in which it was sterilized, and protect from contamination." See U.S.P. XII, p. 65.

Aqua Redestillata—Page 414: In title change "N.F. VI" to "N.F. VII" and delete synonym "Triple-distilled Water." Substitute for first three lines "Redistilled Water contains not more than negligible amounts of oxidizable matter, nonvolatile matter or gases." In last line of *Summarized Description* change "N.F., p. 53" to "N.F. VII, p. 54."

Argentum Proteinicum Mite—Page 627: First paragraph, change "25 per cent of Ag" to "23 per cent of Ag." Change U.S.P. page references to "U.S.P. XII, pp. 69–70."

Arseni Trioxidum—Page 581: Change synonyms to "Arsenious Acid" and "Arsenious Oxide." In second line, change "99.8" to "99.5." Change "Summarized Description" to read: "White, odorless powder; extremely poisonous; stable in air; slowly soluble in water; slightly soluble in alcohol and in ether; freely soluble in glycerin; soluble in hydrochloric acid and in solutions of alkali hydroxides and carbonates." See U.S.P. XII, pp. 70–71.

Arsphenamina—Page 784: Change molecular weight to 475.01. Substitute the following definition: Arsphenamine contains not less than 30 per cent and not more than 32 per cent of arsenic (As). Arsphenamine must be prepared in an establishment licensed for the purpose by the United States Government upon recommendation of the Surgeon General of the United States Public Health Service. Each lot of the product before being offered for sale must comply with the toxicity, labeling, and other requirements of the National Institute of Health, and be released by the Institute. Change dosage from 400 mg. to 0.3 Gm. (5 grains) and add "Prior to injection the solution must be alkalinized with 0.85 cc. of normal sodium hydroxide for each 0.1 Gm. of Arsphenamine." For *identification, tests for purity, assay for arsenic* and *labeling,* see U.S.P. XII, pp. 71–72.

Asafœtida—Page 876: In first line, change "gum-resin" to "oleo-gum-resin." Change U.S.P. page references to "N.F. VII, p. 59."

Aspidium—Page 855: Substitute the following definition from U.S.P. XII for first paragraph: Aspidium consists of the rhizome and stipes of *Dryopteris Filix-mas* (Linné) Schott, known in commerce as European Aspidium or Male Fern, or of *Dryopteris marginalis* (Linné) Asa Gray, known in commerce as American Aspidium or Marginal Fern (Fam. *Polypodiaceæ*). Add to second paragraph "It yields not more than 2 per cent of foreign organic matter."

Atropina—Page 908: Change source to "An alkaloid usually obtained from *Atropa Belladonna* Linné and from species of *Datura* and *Hyoscyamus* (Fam. *Solanaceæ*)." Change U.S.P. page references to "U.S.P. XII, pp. 73–74."

Balsamum Peruvianum—Page 865: In first sentence, change "*Toluifera Pereiræ* (Royle) Baillon" to "*Myroxylon Pereiræ* (Royle) Klotzsch." In *Summarized Description,* change "U.S.P., p. 79" to "U.S.P. XII, p. 76."

Balsamum Tolutanum—Page 866: In first sentence, change "*Toluifera Balsamum* (Linné)" to "*Myroxylon Balsamum* (Linné) Harms." In *Summarized Description,* change "U.S.P., p. 80" to "U.S.P. XII, p. 77."

Barbitalum Solubile—Page 757: Change title to "Barbitalum Sodicum"—Barbital Sodium. Change molecular weight to 206.18. Substitute for first paragraph: Barbital Sodium contains not less than 88 per cent and not more than 90 per cent of barbital ($C_8H_{12}N_2O_3$), calculated on a moisture-free basis, the moisture being determined on a separate portion by drying at 100° C. for three hours. *Storage.*—Preserve in well-closed containers. For *identification, tests for purity* and *assay,* see U.S.P. XII, pp. 78–79.

Betanaphthol—Page 889: Change "Dose" to "0.12 Gm. (2 grains)." Change U.S.P. page references to "U.S.P. XII, p. 85."

Bismuthi Subcarbonas—Page 601: In first sentence, delete "to constant weight at 100° C." and insert in its place "over sulfuric acid for 18 hours." Change U.S.P. page references to "U.S.P. XII, pp. 86–87."

Bismuthi Subgallas—Page 602: This monograph is now in N.F. VII. In first sentence change the words "to constant weight" to "for three hours." For further *description, identification, tests for purity* and *assay,* see N.F. VII, pp. 63–64.

Bismuthi Subsalicylas—Page 602: In first sentence change words "to constant weight at 100° C." to "over sulfuric acid for 18 hours." In first sentence of description change word "crystalline" to "microcrystalline, odorless" and add to description "stable in air, but is affected by light." Change "Dose" to "Gastro-intestinal, 1 Gm. (15 grains); anti-syphilitic, intramuscular in oil, 0.1 Gm. (1½ grains)." Change U.S.P. page references to "U.S.P. XII, pp. 88–89."

Caffeina Citrata—Page 761: Add to first sentence: "and not less than 48 per cent and not more than 52 per cent of anhydrous citric acid ($H_3C_6H_5O_7$). The sum of the percentages of anhydrous caffeine and anhydrous citric acid is not less than 98.5 and not more than 101." Change U.S.P. page references to "U.S.P. XII, pp. 92–93."

Caffeina cum Sodii Benzoate—Page 761: Change title to "Caffeina et Sodii Benzoas." Add to first paragraph: "The sum of the percentages of anhydrous caffeine and sodium benzoate is not less than 98 and not more than 102." Change "Dose" to "Oral or intramuscular, 0.5 Gm. (7½ grains)." Change U.S.P. page references to "U.S.P. XII, pp. 93–94."

Calcii Carbonas Præcipitatus—Page 524: In second line, change "98" to "98.5." Add "*Storage*—Preserve in well-closed containers." Change U.S.P. page references to "U.S.P. XII, pp. 94–95."

Calcii Chloridum—Page 526: In second line, change "85" to "81" and in third line, change "air-tight" to "tight." After "Dose" insert "Intravenous." Change U.S.P. page references to "U.S.P. XII, p. 96."

Calcii Gluconas—Page 696: Change first paragraph to read: "Calcium Gluconate contains not less than 8.8 per cent and not more than 9.3 per cent of calcium (Ca), corresponding to not less than 99 per cent of $Ca(C_6H_{11}O_7)_2.H_2O$." Change U.S.P. page references to "U.S.P. XII, pp. 96–97."

Capsicum—Page 859: Substitute for first sentence "Capsicum is the dried ripe fruit of *Capsicum frutescens* Linné, known in commerce as African Chillies, or of *Capsicum annuum* Linné var. *conoides* Irish, known in commerce as Tabasco Pepper, or of *Capsicum annuum* var. *longum* Sendt, known in commerce as Louisiana Long Pepper, or of a hybrid between the Honka variety of Japanese Capsicum and the Old Louisiana Sport Capsicum known in commerce as Louisiana Sport Pepper (Fam. *Solanaceæ*)." Capsicum must be labeled to indicate which of the above varieties is contained in the package. See N.F. VII, pp. 79–80.

Carbo Activatus—Page 434: *Dose* has been deleted in U.S.P. XII. For *tests for purity* and *adsorptive power*, see U.S.P. XII, pp. 117–118.

Carbonei Tetrachloridum—Page 648: Change "Dose" to "Caution! As an anthelmintic for adults, single dose, 1 cc. (15 minims)." Change U.S.P. page references to "U.S.P. XII, p. 120."

Caryophyllus—Page 848: In first sentence, change "*Caryophyllus aromaticus* Linné" to "*Eugenia caryophyllata* Thunberg." Add to second paragraph "Clove yields, from each 100 Gm., not less than 16 cc. of oil of clove." In second line of the paragraph, delete "and yields not less than 15 per cent of volatile ether-soluble extractive." The dose does not appear in U.S.P. XII.

Cerii Oxalas—Page 549: Change the second line of paragraph to read "a mixture of the oxalates of cerium, neodymium, praseodymium, lanthanum, and other associated elements." For *identification* and *tests for purity*, see N.F. VII, p. 87.

Chionanthus—Fringe Tree Bark: This is not mentioned in "Principles of Pharmacy." It is official in N.F. VII and is the dried bark of the root of *Chionanthus virginicus* Linné (Fam. *Oleaceæ*). It contains a bitter glucoside, chionanthin, and is used as a bitter tonic, diuretic and aperient in doses of 2 Gm. (30 grains).

Chromii Trioxidum—Page 550: In first line, change "95" to "98." Change "Storage" to "Preserve in tight containers." Change U.S.P. page references to "U.S.P. XII, p. 135."

Chrysarobinum—Page 896: In first sentence, change "*Vouacapoua Araroba* (Aguiar) Druce" to "*Andira Araroba* Aguiar." In *Summarized Description*, change "U.S.P., p. 121" to "U.S.P. XII, p. 135."

Cinnamomum—Page 845: Change second sentence to read: "Cinnamon yields, from each 100 Gm., not less than 2.5 cc. of oil of cinnamon and contains not more than 2 per cent of foreign organic matter." There is no dose given in U.S.P. XII. Change U.S.P. page references to "U.S.P. XII, pp. 136–137."

Cocaine—Page 910: Add to first sentence: "or by synthesis from ecgonine or its derivatives." The dose has been deleted from U.S.P. XII. Change U.S.P page references to "U.S.P. XII, pp. 137–138."

Collodium—Page 233: At beginning of monograph insert sentence: "Collodion contains not less than 5 per cent of pyroxylin." Change U.S.P. page references to "U.S.P. XII, p. 144."

Collodium Salicylicum Compositum—Page 234: Change title to "Collodium Salicylicum." Delete Fluidextract of Cannabis from formula in table of "Collodions of the National Formulary."

Colocynthis—Page 721: In sixth line of monograph change "6 per cent" to "4 per cent."

Condurango—Condurango Bark: This is not mentioned in "Principles of Pharmacy." It is official in N.F. VII and is the dried bark of *Marsdenia Condurango* Reichenbach filius (Fam. *Asclepiadaceæ*). It contains glucosides and is used as an aromatic bitter in doses of 4 Gm. (60 grains).

Convallariæ Radix—Page 717: Change title to "Convallaria." Change "Dose" from "0.2 Gm. (3 gr.)" to "30 mg. (½ gr.)." Add "it possesses a potency such that 0.1 Gm. of it is equivalent to not less than 3 U.S.P. XII Digitalis units."

Copaiba—Page 865: In first line, change "*Copaiba*" to "*Copaifera* (*Copaiba*)." Change U.S.P. page references to "N.F. VII, pp. 100–101."

Dextrosum—Page 695: Correct solubility in alcohol to "and in about 60 parts of alcohol." Under "Remarks" add the following: "Note.—In preparing Dextrose Injections it is permissible to use a dextrose which does not conform to the official requirements for water of hydration, provided the product meets all other official requirements for purity and also provided suitable allowance is made for the difference in water content. If such a solution is labeled with respect to its dextrose content, the label should indicate the number of Gm. of U.S.P. (hydrous) Dextrose contained in each 100 cc." See U.S.P. XII, pp. 149 and 150.

Digitalis—Page 718: In third line, delete "possess an activity" and insert in its place "be." In fourth line, delete balance of paragraph after word "Unit" and substitute: "represents the potency of 0.1 Gm. of the U.S.P. Digitalis Reference Standard (U.S.P. XII, p. 607)." In first line, on page 719, change "8" to "6." Add to "Storage" this sentence: "A suitable cartridge or device, containing a non-liquefying, inert, dehydrating substance may be used in the container to maintain low humidity." See U.S.P. XII, pp. 150–151.

Digitalis Pulverata—Page 719: Change second paragraph to read: "The potency of Powdered Digitalis shall be such that, when assayed as directed, 0.1 Gm. shall be equivalent to 1.0 U.S.P. Digitalis Unit (see U.S.P. XII, p. 150)." Add to "Note" this statement: "The attention of physicians is called to the fact that U.S.P. XII Powdered Digitalis is materially reduced in potency when compared with the U.S.P. XI powder." Change "Storage" to "Preserve in water-proof, air-tight, light-resistant containers. A suitable cartridge or device, containing a non-liquefying, inert, dehydrating substance may be used in the container to maintain low humidity." See U.S.P. XII, pp. 151–152.

Elixir Aminopyrinæ—Page 228: The First Supplement to N.F. VII suggests the use of 10 cc. of Compound Solution of Amaranth (see Liquor Amaranthi Compositus in this supplement) in place of the Compound Tincture of Cudbear.

Elixir Ammonii Valeratis—Page 228: The First Supplement to N.F. VII suggests the use of 30 cc. of Compound Solution of Amaranth (see Liquor Amaranthi Compositus in this supplement) in place of the 16 cc. of Compound Tincture of Cudbear.

Elixir Aromaticum Rubrum—Page 228: The First Supplement to N.F. VII suggests dissolving 2.5 Gm. of Amaranth in 1000 cc. of Aromatic Elixir in place of the Tincture of Cudbear.

Elixir Cinchonæ Alkaloidorum—Pages 227 and 229: The First Supplement to N.F. VII suggests the use of 50 cc. of Compound Solution of Amaranth (see Liquor Amaranthi Compositus in this supplement) in place of the Compound Tincture of Cudbear.

Elixir Ferri, Quininæ et Strychninæ—Page 229: The First Supplement to N.F. VII recognizes, until further notice, Elixir Ferri et Strychninæ as a replacement formula due to the restrictions placed on the use of Quinine. The only change in the formula in N.F. VII is to delete the Quinine Hydrochloride. The Second Supplement, issued later, permits, until further notice, the omission of the glycerin.

Elixir Ferri, Quininæ et Strychninæ Phosphatum—Pages 227 and 229: The First Supplement to N.F. VII recognizes, until further notice, Elixir Ferri et Strychninæ Phosphatum as a replacement formula due to the restrictions placed on the use of Quinine. The only change in the formula in N.F. VII is to delete the Quinine Phosphate. The Second Supplement, issued later, permits, until further notice, the omission of the glycerin.

Elixir Glycerophosphatum Compositum—Page 229: The First Supplement to N.F. VII permits the omission of Quinine Hydrochloride from the formula until further notice.

Elixir Iso-Alcoholicum—Page 227: In thirteenth line of monograph change "page 118" to "page 130." In line 14 change "10 to 95 per cent" to "0 per cent to 70 per cent or more." The sentence beginning in line 14 should read "For single liquid galenicals, employ an elixir of an alcoholic strength approximately equivalent to that of the galenical."

Elixir Pepsini—Page 230: The Second Supplement to N.F. VII permits, until further notice, a reduction in the quantity of glycerin in this formula from 200 cc. to 120 cc., with the addition of 45 Gm. of sucrose For revised formula and directions for preparation, see Second Supplement to N.F. VII.

Elixir Pepsini Compositum—Page 230: The First Supplement to N.F. VII suggests the use of 10 cc. of a 5 per cent solution of amaranth in place of the Tincture of Cudbear. The Second Supplement permits, until further notice, the use of a formula in which the glycerin is reduced from 250 cc. to 120 cc., the oil of orange is increased from 2 cc. to 14 cc., and 70 Gm. of sucrose is added. For revised formula and directions for preparation, see Second Supplement to N.F. VII.

Elixir Pepsini et Rennini—Page 230: The Second Supplement to N.F. VII permits, until further notice, a reduction in the quantity of glycerin in this formula from 150 cc. to 120 cc., with the addition of 17 Gm. of sucrose. For revised formula and directions for preparation, see Second Supplement to N.F. VII.

Elixir Terpini Hydratis—Page 230: The Second Supplement to N.F. VII permits, until further notice, a reduction in the quantity of glycerin in this formula from 400 cc. to 200 cc., with an increase in the quantity of alcohol from 425 cc. to 475 cc., and the addition of 185 Gm. of sucrose in place of the 100 cc. of syrup. For revised formula and directions for preparation, see Second Supplement to N.F. VII. The "Storage" is also changed to "Preserve in tight containers at a temperature above 7° C." and the "Alcohol Content" is changed to "43 to 47 per cent by volume."

Emetinæ Hydrochloridum—Page 924: Change first sentence to read: "A hydrated hydrochloride of an alkaloid obtained from ipecac or prepared synthetically by methylation of cephaëline." Change U.S.P. page references to "U.S.P. XII, p. 156."

Emplastrum Adhæsivum—Page 377: This monograph has been extensively revised. Substitute following description: "Adhesive Plaster consists of a mixture, having pressure-sensitive adhesive properties, spread evenly upon fabric, the back of which may be coated with a water-repellent film. The plaster mass must be free from lumps. The plaster must have a tensile strength, determined warpwise, of not less than 20.41 Kg. (45 pounds) per 2.55 cm. (1 inch) of width. *Storage*—Preserve preferably at a temperature not above 30° C. and do not expose to sunlight." For further details, see U.S.P. XII, p. 157.

Emplastrum Belladonnæ—Page 377: In the first paragraph change the last words to read: "alkaloids of belladonna root." Under "Assay" change "U.S.P., p. 140" to read: "U.S.P. XII, p. 158."

Emulsions—Page 281: For new material, see "Emulsa," U.S.P. XII, pp. 159–160.

Emulsum Olei Morrhuæ—Page 287: Change *Dose* to read as follows: "Average daily dose, infants and adults, 15 cc. (4 fluidrachms). Note—Emulsion of Cod Liver Oil prepared from Oil containing more than the minimum U.S.P. requirements for both Vitamin A and Vitamin D may be administered in proportionally smaller doses." See U.S.P. XII, p. 160.

Ephedrina—Page 932: Change the first paragraph to read as follows: "An alkaloid obtained from *Ephedra equisetina* Bunge, *Ephedra sinica* Stapf, and other species of *Ephedra* (Fam. *Gnetaceæ*), or produced synthetically. It is anhydrous, or contains not more than one-half molecule of water of hydration. Anhydrous Ephedrine contains not less than 98.5 per cent of $C_{10}H_{15}NO$. Hydrated Ephedrine contains not less than 94 per cent $C_{10}H_{15}NO$. Change U.S.P. page references to "U.S.P. XII, pp. 161–162."

Ephedrinæ Hydrochloridum—Page 933: In first line change "twenty-four hours" to "eighteen hours." Change solubility in alcohol to "and about 14 parts of alcohol" and add "melts 216°–220° C." Change U.S.P. page references to "U.S.P. XII, pp. 162–163."

Ephedrinæ Sulfas—Page 933: In first line change "twenty-four hours" to "eighteen hours." The melting point is to be omitted as a test for identity. Change U.S.P. page references to "U.S.P. XII, pp. 163–164."

Ergosterol Activatum in Oleo—Pages 210 and 957: Official in U.S.P. XII as Oleovitamina D Synthetica. See page 73 of this supplement under "Liquor Ergosterolis Irradiati."

Ergota—Page 941: In fourth line change "ergotoxine ethanesulfonate" to "U.S.P. Ergotoxine Ethanesulfonate Reference Standard." In the line five change "8" to "6." The First U.S.P. XII Sheet Supplement permits the following modification in storage: "Preserve under all conditions of storage and transportation in water-proof and air-tight containers, provided that temporarily and until rescinded no objection will be registered to the entry into the United States of Ergot not packed or stored in water-proof and in air-tight containers, even though containing more than 8 per cent of moisture, on the condition that it be dried, assayed, and repackaged immediately after entry so as to comply with all of the requirements above set forth." The dose does not appear in U.S.P. XII. Change U.S.P. page references to "U.S.P. XII, pp. 166–167."

Erythritylis Tetranitras Dilutus—Page 682: Official in U.S.P. XII as Tabellæ Erythritylis Tetranitratis. This monograph has been completely rewritten. See page 42 of this supplement and also page 469 of U.S.P. XII.

Extracts—Pages 294–299: For new material, see "Extracta," U.S.P. XII, pp. 174–175, and N.F. VII, pp. 149–150.

Extractum Aloes—Page 304: In table of "Extracts of the National Formulary" in the column headed "strength," cross out the statement "200 per cent of the drug."

Extractum Belladonnæ—Page 297: In the Table of Official Assayed Soft Extracts under "Assayed Standard" change Extract of Belladonna to read: "1.15 to 1.35 per cent."

Page 298: In the Table of Official Assayed Powdered Extracts under "Assayed Standard" change Extract of Belladonna to read: "1.15 to 1.35 per cent."

Page 299: In the first paragraph the standard is changed to read: "not less than 1.15 Gm. and not more than 1.35 Gm. of the alkaloids of belladonna leaf." Under "The Powdered Extract" in the *Condensed Recipe*, change "the extract *must* be defatted" to "the extract *may* be defatted." Change the last sentence of this paragraph to read: "For details see U.S.P. XII, p. 176."

Page 1021: Under "Outline of Assay of Pilular Extract of Belladonna" and "The Assay of Powdered Extract of Belladonna" the sentences reading "For minor variations and other details, see U.S.P., pp. 154 and 155" should read: "See U.S.P. XII, p. 176." That portion of the assay appearing in Principles of Pharmacy has been changed also.

Extractum Digitalis—Page 304: In table of Extracts of the National Formulary in the column headed "strength," change from "350 per cent of drug" to "300 per cent of drug." See N.F. VII, pp. 152–153.

Extractum Ergotæ—Page 304: In table of Extracts of the National Formulary in the column headed "diluent" change "starch or glycerin" to "suitable diluent." In the column headed "strength," cross out the word "about." See N.F. VII, p. 153.

Extractum Fellis Bovis—Page 300: Change first sentence to: "Extract of Ox Bile contains an amount of the sodium salts of ox bile acids equivalent to not less than 45 per cent of cholic acid ($C_{24}H_{40}O_5$)." The "Preparation" does not appear in U.S.P. XII and the monograph has been completely rewritten. Insert "*Summarized Description*—Brownish yellow, greenish yellow or brown powder; bitter taste; soluble in water and in alcohol; solutions foam strongly when shaken." Insert "*Storage*—Preserve in tight containers." and change "Dose" to "0.3 Gm. (5 grains)." For complete monograph, see U.S.P. XII, pp. 177–178.

Extractum Glycyrrhizæ Purum—Page 301: The preparation has been changed in U.S.P. XII in that enough solution of ammonia is added to the percolate before evaporation to impart a distinctly ammoniacal odor. Change U.S.P. page reference to "U.S.P. XII, p. 178."

Extractum Hepatis—Page 965: Change first paragraph to read: "Extract of Liver is a dry, brownish, somewhat hygroscopic powder, and contains that soluble thermostable fraction of mammalian livers which increases the number of red blood corpuscles in the blood of persons suffering from pernicious anemia. The approximate antianemic potency of Extract of Liver in pernicious anemia shall be expressed in U.S.P. Units and shall conform to all other provisions outlined under *Anti-anemia Preparations,* U.S.P. XII, p. 553." Change "Storage" to "Preserve in well-closed containers, preferably at a temperature not above 20° C." and change "Dose" to "One U.S.P. Unit."

Extractum Hyoscyami—Page 301: The last line of the paragraph headed "Condensed Recipe" should read: "For details see U.S.P. XII, pp. 179–180. Change apothecaries' dose "⅚ grain" to "¾ grain."

Extractum Malti—Page 301: Under "Remarks," change "U.S.P. XI" in the third sentence to read: "U.S.P. XII."

Extractum Nucis Vomicæ—Page 302: Under "Condensed Recipe" change "For details see U.S.P., p. 160" to "For details see N.F. VII, pp. 155–156." The procedure as outlined in Principles of Pharmacy has been changed somewhat when this extract was transferred to the National Formulary.

Extractum Stramonii—Page 297: In the Table of Official Assayed Soft Extracts under "Assayed Standard" change "Extract of stramonium" to read: "0.90 to 1.10 per cent."

Page 298: In the table of Official Assayed Powdered Extracts under "Assayed Standard" change "Extract of stramonium" to read: "0.90 to 1.10 per cent."

Page 302: In the first paragraph the standard should read "not less than 0.90 Gm. and not more than 1.10 Gm. of the alkaloids of stramonium." In the second paragraph change the last sentence to read: "See U.S.P. VII, pp. 182–183."

Ferri et Ammonii Citrates—Page 575: Change "Dose" to "1 Gm. (15 grains)." Change U.S.P. page references to "U.S.P. XII, pp. 183–184."

Ferri Sulfas—Page 564: Change "Dose" to "0.3 Gm. (5 grains)." Change U.S.P. page references to "U.S.P. XII, pp. 185–186."

Fluidextracta—Page 263: Add the following note to the paragraph headed "Preservation of Fluidextracts": "A fluidextract which may deposit sediment may be aged and filtered or the clear portion decanted, provided that the resulting clear liquid conforms to the official standards."

Pages 259, 260, 261 and 262: In the general processes of manufacture described as Process A, B, C, and D, respectively, in place of adding "sufficient menstruum," it is now directed that a mixture of alcohol and water be used as the final adjusting or diluting liquid to bring the finished product up to the required volume (1000 cc. in the U.S.P. formula). The proportions of alcohol and water in the mixture must be such, in each case, that the finished product will contain the correct volume of C_2H_5OH provided for in the standard. The reserve percolate and the diluting liquid must be thoroughly mixed in each case. See U.S.P. XII, pp. 187–191. See also N.F. VII, pp. 166–171.

Fluidextractum Apii Fructus—Page 271: In table opposite "Celery Fruit," change "A" to "C" and change the first menstruum to "Alcohol."

Fluidextractum Convallariæ Radicis—Page 274: In table of "Official Fluidextracts Directed to be Assayed Biologically" change title to "Convallaria (N.F. VII)" and change "0.1 Gm." to "0.1 cc." See N.F. VII, p. 179. On page 271 in table opposite "Convallaria root" change the dose in the last column to "0.03 cc. (½ minim)."

Fluidextractum Cubebæ—Page 271: In table opposite "Cubeb," change "A" to "C" and change the first menstruum to "Alcohol."

Fluidextractum Ergotæ—Page 267: The rubric and assay have been deleted from U.S.P. XII. See U.S.P. XII, p. 192.

Fluidextractum Ipecacuanhæ—Page 269: In U.S.P. XII the expectorant dose has been deleted and the emetic dose has been changed to "0.5 cc. (8 minims)." Change U.S.P. page references to "U.S.P. XII, pp. 193–194."

Fluidextractum Juniperi—Page 271: In table opposite "Juniper," change "A" to "C" and change the first menstruum to "Alcohol, 9; water, 1."

Fluidextractum Thymi—Page 271: In table opposite "Thyme," change "B" to "C" and the first menstruum to "Alcohol, 2; water, 1." Delete final menstruum.

Fluidextractum Viburni Opuli—Page 271: In table opposite "Viburnum opulus," change the dose to "4 cc. (60 minims)." See Second Supplement to N.F. VII.

Gambir—Page 812: Change "*Ourouparia Gambir*" to "*Uncaria Gambir.*"

Gelatinum—Page 951: Add to first paragraph: "Gelatin derived from an acid-treated precursor, exhibits an isoelectric point between *p*H 7 and *p*H 9, while Gelatin derived from an alkali-treated precursor has an isoelectric point between *p*H 4.7 and *p*H 5.0." Add "*Storage*—Preserve in well-closed containers in a dry place." Change U.S.P. page references to "U.S.P. XII, pp. 197–198."

Gelatum Ephedrinæ Sulfatis—This N.F. monograph is not mentioned in Principles of Pharmacy. Jelly of Ephedrine Sulfate (Ephedrine Jelly) yields from each 100 Gm. not less than 0.65 Gm. and not more than 0.85 Gm. of anhydrous ephedrine. It consists of ephedrine sulfate, glycerin, tragacanth, methyl salicylate, eucalyptol, oil of dwarf pine needles and distilled water to which sodium phosphate may be added as a stabilizer. The First Supplement to N.F. VII permits the omission of oil of dwarf pine needles from this formula until further notice. See N.F. VII, p. 201.

Gentiana—Page 716: In the third line of monograph change "not more than 10 per cent" to read "not more than 15 per cent." The dose does not appear in U.S.P. XII. See U.S.P. XII, pp. 200–201.

Glyceritum Acidi Tannici—Page 231: In "Condensed Recipe" after "Tannic Acid (20 Gm.)" insert "exsiccated sodium sulfite (0.2 Gm.)" and change "(79 Gm.)" to "(78.8 Gm.)." Change U.S.P. page reference to "U.S.P. XII, pp. 203–204."

Glyceritum Amyli—Page 231: Under "Ingredients," add "benzoic acid, 0 2 Gm." Under "Manipulation," change first part of sentence to read: "The starch and benzoic acid are triturated with the distilled water until smooth and then the glycerin is added." Add "*Storage*—Preserve in tight containers." Change U.S.P. page reference to "U.S.P. XII, p. 204."

Gossypium Purificatum—Page 701: The first paragraph (definition) should read as follows: "The hairs of the seed of cultivated varieties of *Gossypium hirsutum* Linné, or of other species of *Gossypium* (Fam. *Malvaceæ*), freed from adhering impurities, deprived of fatty matter, bleached and sterilized." Insert the following paragraphs:

Storage.—Package Purified Cotton in rolls of not more than 454 Gm. (1 pound) of a continuous lap, with a light-weight paper running under the entire lap, the paper being of such width that it may be folded over the edges of the lap to a distance of at least one inch, the two together being tightly and evenly rolled, and enclosed and sealed in a second well-closed container. Purified Cotton may also be packaged in other types of containers if these are so constructed that the sterility of the product is maintained.

Purified Cotton shall be sterilized in the sealed container, and the container shall bear a statement to the effect that the sterility of the Cotton cannot be guaranteed if the package bears evidence of damage or if the package has been opened previously.

Substitute for "Summarized Description": White, soft, fine filament-like hairs appearing under the microscope as hollow, flattened, and twisted bands, striate and slightly thickened at the edges; nearly odorless; almost tasteless; insoluble in ordinary solvents; soluble in ammoniated cupric oxide T.S.

For *tests for purity* and *other information*, see U.S.P. XII, p. 207.

Hydrargyri Chloridum Mite—Page 616: In first sentence, delete "to constant weight" and insert after word "acid" the phrase "for 18 hours." Change "Dose" to "0.12 Gm. (2 grains)." Change U.S.P. page references to "U.S.P. XII, pp. 211–212."

Hydrargyrum cum Creta—Page 612: Change the sixth line to read: "from 36 to 40 per cent mercury."

Page 613: Change the first sentence to read: "Mercury with Chalk contains not less than 36 per cent and not more than 40 per cent of Hg." See U.S.P. XII, p. 216.

Infusum Sennæ cum Magnesii Sulfate—Page 238: In line 6 of the monograph note that "black draught" has been deleted from the N.F. VII as a synonym.

Page 277: In line 8 of the monograph for Acetum Opii, note that "black draught" has been deleted as a synonym for "Compound Infusion of Senna." See N.F. VII, p. 220.

Ipecacuanha—Pages 933–934: Change dose to "Emetic 0.5 Gm. (7½ gr.)." "Expectorant Dose" does not appear in U.S.P. XII. Change U.S.P. page references to "U.S.P. XII, pp. 252–253."

Iris Versicolor—Blue Flag: This is not mentioned in "Principles of Pharmacy." It is official in N.F. VII and is the dried rhizome of *Iris versicolor* or of *Iris virginica.* It contains a volatile oil and is used as a cathartic and diuretic in doses of 2 Gm. (30 grains).

Jalapa—Page 720: Change the first sentence in the monograph to read as follows: "Jalap is the dried tuberous root of *Exogonium purga* (Wenderoth) Bentham (Fam. *Convolvulaceæ*)." See N.F. VII, p. 223.

Linimentum Chloroformi—Page 291: Change first paragraph to read: "Chloroform Liniment contains, at 25° C., in each 100 cc., not less than 27 cc. and not more than 30.5 cc. of $CHCl_3$." The "Caution" does not appear in U.S.P. XII. Change "Storage" to read: "Preserve in tight containers, preferably at a temperature not above 30° C." Add "*Alcohol Content*—From 43 to 47 per cent, by volume." Change U.S.P. page references to "U.S.P. XII, pp. 256–257."

Linimentum Saponis Mollis—Page 291: In first line under "Condensed Recipe" change "200 cc." to "300 cc." The first U.S.P. XII Sheet Supplement permits the 20 cc. of Oil of Lavender to be replaced by 20 cc. of Oil of Cedar Leaf.

Linum—Page 740: In the second sentence, change the statement "at least 98 per cent of which is saponifiable" to "of which not more than 2 per cent is unsaponifiable matter." For details, see U.S.P. XII, pp. 257–258.

Liquor Amaranthi Compositus: The First Supplement to N.F. VII suggests this formula as a substitute for Compound Tincture of Cudbear where used as a coloring agent in N.F. preparations. It consists of 100 Gm. of caramel dissolved in 700 cc. of distilled water to which is added 35 cc. of a 5 per cent w/v solution of amaranth, 250 cc. of alcohol and enough water to make 1000 cc.

Liquor Aromaticus Alkalinus—Page 213: The First Supplement to N.F. VII suggests the use of 10 cc. of a 5 per cent solution of amaranth in place of the Tincture of Cudbear and the increase of the alcohol from 50 cc. to 60 cc. The Second Supplement to N.F. VII permits, until further notice, the reduction of the quantity of glycerin in this formula from 100 cc. to 50 cc. per liter.

Liquor Cresolis Saponatus—Page 791: This monograph has been extensively revised. Insert following definition: "Saponated Solution of Cresol contains, in each 100 cc., not less than 46 cc. and not more than 52 cc. of cresol. It is prepared by the saponification of a mixture of vegetable oils, excluding coconut and palm kernel oils, and cresol. The vegetable oil may be corn, cottonseed, linseed, or soya bean, or similar oils which have a saponification number not greater than 205 and an iodine value not less than 100." Under "Condensed Recipe" substitute the following: "Mix 350 cc. of the vegetable oil and 55 cc. of alcohol, add a solution of 72.6 Gm. of 85 per cent potassium hydroxide in 100 cc. of distilled water and heat with stirring until saponification is complete. Add 500 cc. of cresol; stir until the solution is clear and add enough distilled water to make 1000 cc. The alcohol may be omitted and, if desired, 58.08 Gm. of the 85 per cent potassium hydroxide may be replaced by 37.05 Gm. of 95 per cent sodium hydroxide. For details and assay, see U.S.P. XII, pp. 264–266."

Liquor Ephedrinæ Sulfatis—Page 213: The N.F. VII formula also contains sodium chloride. See N.F. VII, pp. 245–246.

Liquor Epinephrinæ Hydrochloridi—Page 817: Substitute for the first two paragraphs: "Solution of Epinephrine Hydrochloride is a solution of epinephrine hydrochloride in distilled water, and has a potency equivalent to a solution containing 1 Gm. of U.S.P. Epinephrine Reference Standard in each 1000 cc." Add synonym "Solution of Epinephrine Hydrochloride 1:1000." Change "Storage" to "Preserve in small, well-filled, light-resistant, tight containers." The dose does not appear in U.S.P. XII. Change U.S.P. page reference to "U.S.P. XII, pp. 266–267."

Liquor Ergosterolis Irradiati—Pages 210 and 957: Substitute the following monograph:

OLEOVITAMINA D SYNTHETICA—Synthetic Oleovitamin D

(**Oleovitam. D. Synth.**—Viosterol in Oil (Applying only to Activated Ergosterol in Oil).)

Synthetic Oleovitamin D is a solution of activated ergosterol, or activated 7-dehydro-cholesterol, in an edible vegetable oil. Synthetic Oleovitamin D contains in each Gm. not less than 10,000 U.S.P. Units of Vitamin D.

Synthetic Oleovitamin D must be labeled to indicate whether it contains activated ergosterol (*Vitamin* D_2 or *Viosterol*) or whether it contains activated 7-dehydro-cholesterol (*Vitamin* D_3).

Storage.—Preserve in small, tight containers, preferably in a cold place.

Summarized Description.

Clear, colorless to light yellow, oily liquid; almost odorless; bland taste; slightly soluble in alcohol; miscible with ether and with chloroform.

For ***test for free fatty acids*** and ***assay***, see U.S.P. XII, pp. 312–313.

Remarks.—This is a concentrated source of Vitamin D and is used for prophylaxis and treatment of rickets and other Vitamin D deficiencies. It has advantages over Cod Liver Oil in that it is highly concentrated, odorless, has a bland taste, and if only the Vitamin D is desired does not have the high concentration of Vitamin A. Dry pure viosterol loses its potency rather quickly so it is provided only in this vegetable oil solution.

This preparation may contain either activated ergosterol which is obtained from vegetable sources, or 7-dehydro-cholesterol, which is obtained from animal sources, but must be labeled which is present because there is some doubt as to the identity of their actions in man. Either may be activated by the action of ultraviolet rays.

Dose.—Prophylactic, 0.1 cc. (1½ minims).

Liquor Ferri Chloridi—Page 566: Change "Storage" to "Preserve in tight containers, protected from light, and avoid continuous excessive heat." Change "Summarized Description" to read: "Yellowish brown liquid; faint odor of hydrochloric acid; acid reaction; miscible in all proportions with alcohol; specific gravity, 1.29–1.35." Change U.S.P. page references to "N.F. VII, pp. 246–247 and Second Supplement to N.F. VII."

Liquor Hepatis—Page 965: In first line after word "Liver," insert: "is a brownish liquid, and." After word "soluble," insert "thermostable." In first line, on page 966, delete balance of sentence after word "anemia" and add this sentence: "The approximate anti-anemic potency of Solution of Liver in pernicious anemia is expressed in U.S.P. Units and conforms to all other provisions outlined under *Anti-anemia Preparations*, U.S.P. XII, page 553." Change "Storage" to "Preserve in well-closed containers, preferably at a temperature not above 20° C., and protected from light." Add "*Dose*—One U.S.P. Unit." Change U.S.P. page reference to "U.S.P. XII, p. 268."

Liquor Hepatis Purificatus—Page 966: Appears in U.S.P. XII as "Injectio Hepatis." The monograph has been extensively revised. See U.S.P. XII, p. 230 and "Injectiones" in this supplement.

Liquor Iodi Compositus—Page 210: Change title to "Liquor Iodi Fortis—Strong Solution of Iodine." Change "Storage" to "Preserve in tight containers, preferably at a temperature not above 35° C." Change "Dose" to "0.3 cc. (5 minims)." Change U.S.P. page references to "U.S.P. XII, pp. 270–271."

Liquor Magnesii Citratis—Page 517: Add the following "Note" to the first paragraph: "Dispense Solution of Magnesium Citrate in bottles containing not less than 340 cc. and not more than 360 cc., or in bottles containing not less than 195 cc. and not more than 205 cc." Change "Dose" to "200 cc. (7 fluidounces)" and change the U.S.P. page references to "U.S.P. XII, pp. 271–272."

Liquor Methylrosanilini Chloridi—Page 214: In third column change "Methylrosaniline, 30 Gm." to "Methylrosaniline Chloride, 10 Gm."

Liquor Nucis Vomicæ Alkaloidorum—Page 214: In third column, change "caramel" to "solution of resorcin brown."

Liquor Parathyroidei—Page 962: Appears in U.S.P. XII as "Injectio Parathyroidei." This monograph has been extensively revised. See U.S.P. XII, pp. 240–242 and "Injectiones" in this supplement.

Liquor Pituitarii Posterioris—Page 964: Appears in U.S.P. XII as "Injectio Pituitarii Posterioris." This monograph has been extensively revised. See U.S.P. XII, pp. 244–246 and "Injectiones" in this supplement.

Liquor Sodii Chloridi Physiologicus—Page 211: Change title to "Liquor Sodii Chloridi Isotonicus—Isotonic Solution of Sodium Chloride." This monograph has been extensively revised. Substitute the following:

Isotonic Solution of Sodium Chloride contains, in each 100 cc., not less than 0.88 Gm. and not more than 0.92 Gm. of NaCl. *Unless otherwise specified, No. 3—Sterile Isotonic Solution of Sodium Chloride for Parenteral Use must be dispensed.*

Storage.—Preserve in hermetic or other suitable containers. See "Containers for Injections," U.S.P. XII, page 567.

Condensed Recipe.

No. 1—Non-sterile Isotonic Solution of Sodium Chloride is made by dissolving 9 Gm. of Sodium Chloride in enough distilled water to make 1000 cc., and filtering.

No. 2—Sterile Isotonic Solution of Sodium Chloride Not for Parenteral Use is the No. 1 solution sterilized preferably by Process C, U.S.P. XII, page 614.

No. 3—Sterile Isotonic Solution of Sodium Chloride for Parenteral Use is the No. 1 solution made with water for injection and sterilized preferably by Process C and meeting certain specified requirements as outlined in U.S.P. XII, pp. 274–275.

Summarized Description.

Clear, colorless solution; slightly saline taste; pH of 5 to 7. For *further details, tests for purity* and *assay*, see U.S.P. XII, pp. 274–275.

Note.—Aqueous Solution of Sodium Chloride of a lower or higher concentration of sodium chloride than the official Isotonic Solution of Sodium Chloride must not be dispensed when the Isotonic Solution is prescribed.

The title "Hypotonic Solution of Sodium Chloride" applies to solutions which contain less than 0.88 Gm. of sodium chloride in each 100 cc., and the title "Hypertonic Solution of Sodium Chloride" applies to solutions which contain more than 0.92 Gm. of sodium chloride in each 100 cc., and such solutions should be so labeled when dispensed, and the proportion or the weight of sodium chloride in a given volume must be indicated on the label.

Liquor Sodii Citratis—Page 214: In the table of Solutions of the National Formulary, in the column headed "Remarks," change dose from "8 cc. (2 fluidrachms)" to "15 cc. (4 fluidrachms)." See N.F. VII, pp. 265–266.

Liquor Sodii Hypochloritis—Page 422: Add the statement "*Note*—If 'Labarraque's Solution' is ordered, Solution of Sodium Hypochlorite, diluted with an equal volume of water, is to be dispensed." Change "Storage" to "Preserve in tight, light-resistant containers, preferably at a temperature not above 25° C." Change U.S.P. page references to "U.S.P. XII, pp. 276–277."

Lotio Calaminæ—Page 280: The N.F. VII formula also contains magma of bentonite which was introduced as a suspending agent. See N.F. VII, p. 274.

Magnesii Carbonas—Page 516: Change the first paragraph to read: "Magnesium Carbonate is a basic hydrated magnesium carbonate or a normal hydrated magnesium carbonate. It contains the equivalent of not less than 40.0 per cent and not more than 43.5 per cent of MgO." See U.S.P. XII, p. 280.

Magnesii Oxidum, Magnesii Oxidum Ponderosum—Pages 514–515. Delete second sentence in each monograph. Change laxative dose appearing at end of monograph for Heavy Magnesium Oxide to 4 Gm. (60 gr.). Change U.S.P. page references to "U.S.P. XII, p. 281" and "U.S.P. XII, p. 282," respectively.

Magnesii Sulfas—Page 518: In second line change "45 per cent" to "40 per cent." *Storage.*—Change "Preserve in air-tight containers" to read: "Preserve in well-closed containers." See U.S.P. XII, p. 284.

Massa Ferri Carbonatis—Page 559: Change "Dose" to "0.6 Gm. (10 grains)." Add "*Storage*—Preserve in tight, light-resistant containers." Change U.S.P. page reference to "U.S.P. XII, pp. 286–287."

Massa Hydrargyri—Pages 329 and 612: This article is now official in N.F. VII. The first line under the headings in each case should read as follows: "Mass of Mercury contains not less than 31 per cent and not more than 35 per cent of Hg." See N.F. VII, p. 282.

Menthol—Page 829: Change "Storage" to read: "Preserve in tight containers, preferably at a temperature not above 30° C." Under "Summarized Description" change first part of description to read: "Colorless, hexagonal crystals, usually needle-like or in fused masses, or as a crystalline powder, having a peppermint-like odor," and add "freely soluble in glacial acetic acid." The last sentence in the first paragraph under this heading and the last line of the second paragraph under this heading should read: "See U.S.P. XII, p. 291."

Methenamina—Page 766: Insert after "Methenamine" in first line, "when dried over sulfuric acid for 4 hours." Change "Dose" to "0.5 Gm. (7½ grains)." Change U.S.P. page references to "U.S.P. XII, pp. 292–293."

Methylis Salicylas—Page 800: In first line, after word "by," insert "maceration and subsequent." Change "Storage" to "Preserve in tight containers." The dose does not appear in U.S.P. XII. Change U.S.P. page references to "U.S.P. XII, pp. 293–294."

Methylthioninæ Chloridum—Page 779: Change first paragraph to read as follows: "Methylthionine Chloride contains not less than 98.5 per cent of $C_{16}H_{18}ClN_3S$, calculated on a dry basis, the loss on drying being determined on a separate portion by drying at 110° C. for eighteen hours." Under "Summarized Description" change the words "See U.S.P., p. 235" in the last sentence of the first paragraph and in the second paragraph to read: "See U.S.P. XII, p. 296."

Mistura Cretæ—Page 279: Change "Ingredients" to "Prepared chalk, 6 Gm.; saccharin sodium, 0.03 Gm.; bentonite, 2.5 Gm.; cinnamon water, 40 cc.; distilled water, enough to make 100 cc. Change "Manipulation" to "Sprinkle the bentonite upon 50 cc. of hot distilled water; wet well; allow to stand 10 hours; add cinnamon water and then add magma to mixture of prepared chalk and saccharin sodium in a mortar; finally add enough distilled water to make 100 cc." For alternative method and details, see U.S.P. XII, p. 297.

Mistura Rhei Composita—Page 279: Change title to "Mistura Rhei et Sodæ" in monograph on page 279 and in table on page 280, "Mixtures of the National Formulary." The Second Supplement to N.F. VII permits, until further notice, a reduction in the quantity of glycerin in this formula from 200 cc. to 160 cc. per liter.

Morphinæ Sulfas—Page 926: Change molecular weight to 758.82. The definition does not appear in U.S.P. XII. Change "Storage" to read: "Preserve in tight, light-resistant containers." Change "Summarized Description" to read: "White, feathery, silky crystals, cubical masses of crystals, or white, crystalline powder; odorless; when exposed to air gradually loses water of hydration; affected by light; soluble in 16 parts of water and in 570 parts of alcohol; soluble in 1 part of water at 80° C. and in about 240 parts of alcohol at 60° C.; insoluble in chloroform and in ether. For *identification* and *tests for purity,* see U.S.P. XII, pp. 297–298. Change the dose to "10 mg. (1/6 grain)."

Mucilago Acaciæ—Page 215: In third line under "Condensed Recipe," change "One Gm." to "Two Gm." Add to monograph: "*Storage*—Preserve in well-closed containers." Change U.S.P. page reference to U.S.P. XII, pp. 298–299."

Mucilago Tragacanthæ—Page 215: Add to "Ingredients," "benzoic acid, 0.2 Gm." This is to be dissolved in the hot water to which the tragacanth is added. Add to monograph: "*Storage*—Preserve in well-closed containers." Change U.S.P. page reference to "U.S.P. XII, p. 299."

Myrrha—Page 877: In first sentence, change "gum resin" to "oleogum-resin" and insert "*Commiphora molmol Engler,*" after words "obtained from."

Neoarsphenamina—Page 785: The structural formula does not appear in U.S.P. XII. Substitute for first paragraph: "Neoarsphenamine consists chiefly of sodium 3,3′-diamino-4,4′-dihydroxyarsenobenzene-N-methanal sulfoxylate. It contains not less than 19 per cent of arsenic (As). Neoarsphenamine must be prepared in an establishment licensed for the purpose by the United States Government upon recommendation of the Surgeon General of the United States Public Health Service. Each lot of the product being offered for sale must comply with the toxicity, labeling, and other requirements of the National Institute of Health, and be released by the Institute. *Caution*—Solutions of Neoarsphenamine must be freshly prepared when required for use. The solution should not be shaken during its preparation." In "Storage" change "10° C." to "20° C." Change "Dose" to "Intravenous, 0.45 Gm. (7 grains)." Change U.S.P. page references to "U.S.P. XII, pp. 301–303."

Neocinchophenum—Page 899: The definition does not appear in U.S.P. XII. Change "Dose" to "0.3 Gm. (5 grains)." Add to monograph: "*Storage*—Preserve in well-closed, light-resistant containers." Change U.S.P. page references to "U.S.P. XII, p. 303."

Oleatum Hydrargyri—Page 234: Change first paragraph to read: "Oleate of Mercury contains the equivalent of not less than 24 per cent and not more than 26 per cent of HgO. *Caution*—Oleate of Mercury must not be dispensed if globules of mercury have separated." Change "Storage" to read: "Preserve in tight, light-resistant containers." Change U.S.P. page references to "U.S.P. XII, pp. 308–309."

Oleovitamina D Synthetica—See "Liquor Ergosterolis Irradiati" in this supplement.

Oleum Amygdalæ Amaræ—Page 793: In first line of second paragraph, change "95" to "80." Under "Summarized Description," change refractive index to "1.5410–1.5442." Change "Storage" to "Preserve in well-filled, tight containers and avoid exposure to excessive heat." Change U.S.P. page references to "U.S.P. XII, pp. 313–314."

Oleum Amygdalæ Expressum—Page 731: Under "Summarized Description" the Saponification Number should read "190 to 200" and the "Iodine Absorption Number" should read "95 to 105." Change U.S.P. page references to "U.S.P. XII, pp. 314–315."

Oleum Betulæ Empyreumaticum Rectificatum—Rectified Oil of Birch Tar—Ol. Bet. Empyr. Rect. (Oleum Rusci). Insert on page 864 this monograph. Rectified Oil of Birch is the pyroligneous oil obtained by the dry distillation of the bark and wood of *Betula pendula* Roth and related species of *Betula* (Fam. *Betulaceæ*), and rectified by steam distillation. It is a limpid, dark brown liquid with a penetrating, empyreumatic odor; yields clear mixtures with 3 volumes of dehydrated alcohol, and with ether, chloroform, glacial acetic acid, amyl alcohol, oil of turpentine, and benzene. For further information see N.F. VII, p. 300–301. It is an ingredient in Compound Ointment of Resorcinol N.F. VII. However, the First Supplement to N.F. VII permits until further notice the replacement of the Rectified Oil of Birch Tar by 2 Gm. of Juniper Tar.

Oleum Caryophylli—Page 849: In first paragraph, change "*Caryophyllus aromaticus* Linné" to "*Eugenia caryophyllata* Thunberg." In last line of "Outline of Assay" change "U.S.P., p. 250" to "U.S.P. XII, pp. 316–317."

Oleum Chenopodii—Page 841: Change second paragraph to read: "It contains not less than 65 per cent, by weight, of ascaridol, $C_{10}H_{16}O_2$" Insert before the dose the statement "Caution! As an anthelmintic for adults, single dose." Change U.S.P. page references to "U.S.P. XII, pp. 318–319."

Oleum Gossypii Seminis—Page 732: In first paragraph, change "*herbaceum*" to "*hirsutum*." Change "Storage" to "Preserve in tight containers." In "Summarized Description," change "U.S.P., p. 225" to "U.S.P. XII, p. 322."

Oleum Iodatum—Page 731: In first sentence, change "39" to "38" and "41" to "42." Add "*Storage*—Preserve in well-filled, tight, light-resistant containers." Change U.S.P. page references to "U.S.P. XII, pp. 323–324."

Oleum Lavandulæ—Page 842: In first paragraph, change "*Lavandula Spica* Linné (*Lavandula officinalis* Chaix, *Lavandula vera* DeCandolle)" to "*Lavandula officinalis* Chaix et Villars (*Lavandula vera* DeCandolle)." In "Summarized Description," change "U.S.P., p. 257" to "U.S.P. XII, p. 325." Change "Storage" to "Preserve in tight containers." The dose is deleted in U.S.P. XII. The First Supplement to N.F. VII permits until further notice the use of an equal volume of Oil of Cedar Leaf U.S.P. in all N.F. preparations for external use in which oil of lavender is an ingredient.

Oleum Menthæ Piperitæ—Page 847: In second line, delete "steam" and add at end of sentence: "and neither partially nor wholly dementholized." Under "Summarized Description" change refractive index to "1.4590 to 1.4650." Change "Storage" to "Preserve in tight containers." The dose does not appear in U.S.P. XII. Change U.S.P. page references to "U.S.P. XII, pp. 327–328."

Oleum Morrhuæ—Page 736: Change sentence at top of page 737 to read: "Cod Liver Oil contains in each Gm. not less than 850 U.S.P. Units of Vitamin A and not less than 85 U.S.P. Units of Vitamin D." Change U.S.P. references to pages 329 and 330.

Oleum Morrhuæ Non-Destearinatum—Page 737: In the third line of the first paragraph, change "600" to "850."

Oleum Pini Pumilionis—Page 863: First paragraph, change "*Pinus montana* Miller (*Pinus pumilio* Haenke)" to "*Pinus Mugo* Turra (*Pinus Pumilio* Haenke)." Second paragraph, change "5 per cent of esters" to "4 per cent of esters." Change "Storage" to "Preserve in tight containers." In "Summarized Description," change "U.S.P., p. 265" to "U.S.P. XII, p. 334."

Oleum Rosæ—Page 842: First paragraph, after "*Rosa damascena* Miller" add "*Rosa alba*, Linné, and *Rosa centifolia* Linné." Change "Storage" to "Preserve in well-filled, tight containers." Change in next to last line page 842, "U.S.P., p. 266" to "U.S.P. XII, p. 335" and delete last line.

Oleum Rosmarini—Page 843: In third line, change "2.5" to "1.5." Change "Storage" to "Preserve in well-filled, tight containers and avoid exposure to excessive heat." The dose does not appear in U.S P. XII. Change U.S.P. page references to "U.S.P. XII, pp. 335–336."

Oleum Sassafras—Page 845: First paragraph, change "*Sassafras variifolium* (Salisbury) O. Kuntze" to "*Sassafras albidum* (Nuttall) Nees." Change "Storage" to "Preserve in tight containers." In last line of Summarized Description," change "U.S.P., p. 268" to "U.S.P. XII, p. 336." The dose does not appear in U.S.P. XII.

Ovarii—Page 967: Change the title "Ovarii" to "Ovarium."

Pancreatinum—Page 953: In first sentence change "amylopsin, trypsin, and steapsin" to "pancreatic amylase, trypsin, and pancreatic lipase." Change "Storage" to read: "Preserve in tight containers, preferably at a temperature not above 30° C." Change U.S.P. references in monograph to pages 346 and 347.

Paraldehydum—Page 665: The definition does not appear in U.S.P. XII. Change "Storage" to "Preserve in well-filled, tight, light-resistant containers which hold not more than 120 Gm., preferably at a temperature not above 30° C." Change boiling point to "distils between 120° and 126° C" Change "Dose" to "4 cc. (1 fluidrachm)" and change U.S.P. page references to "U.S.P. XII, pp. 347–348."

Pelletierinæ Tannas—Page 907: Insert after "mixture," in the first line, "in varying proportions." Add after first sentence: "It contains an amount of the alkaloids equivalent to not less than 20 per cent as the hydrochloride." Change "Storage" to "Preserve in tight, light-resistant containers." Change U.S.P. page references to "U.S.P. XII, pp. 348–349."

Persio—Pages 777 and 882: Cudbear is a powder prepared from species of *Roccella* DeCandolle, *Lecanora* Acharius, or other lichens (Fam. *Parmeliaceæ*) and yields not more than 12 per cent of total ash. The First Supplement to N.F. VII directs that Amaranth may be substituted for Persio in N.F. preparations colored with this coloring agent. The amount used should be that amount which will reasonably simulate the color when cudbear is used. In some cases it may be necessary to adjust the alcoholic content.

Petrolatum Liquidum—Page 642: Under "Synonyms" add "Heavy Liquid Petrolatum." Under "Summarized Description" change the second sentence to read as follows: "The heavy has a kinematic viscosity of not less than 38.1 centistokes at 37.8° C., the light has a kinematic viscosity of not more than 37 centistokes at 37.8° C." Insert "The specific gravity of the heavy oil is 0.860 to 0.905."
Page 643: In the second line on this page, change "U.S.P., p. 281" to read: "U.S.P. XII, p. 353."

Petrolatum Liquidum Leve—Page 642: This is a new title to distinguish the light oil from the heavy. The English title is "Light Liquid Petrolatum" (Petrolat. Liq. Lev.—Light Liquid Paraffin, Light White Mineral Oil). The definition, storage, description and physical properties, tests for identity and impurities, are the same as for Petrolatum Liquidum but specific gravity and kinematic viscosity differ. The specific gravity is 0.828 to 0.880 and kinematic viscosity is not more than 37 centistokes at 37.8° C. See U.S.P. XII, p. 354.

Phenacainæ Hydrochloridum—[illegible] 913: The definition does not appear in U.S.P. XII. Add "Phenacaine Hy[illegible]chloride, when dried at 105° C. for 6 hours, contains not less than 87.5 pe[illegible]nt and not more than 90.5 per cent of phenacaine base ($C_{18}H_{22}N_2O_2$)." Ch[illegible]e U.S.P. page references to "U.S.P. XII, pp. 354–355."

Phenobarbitalum Solubile—[illegible]e 758: Change title to "Phenobarbitalum Sodicum—Phenobarbital Sodium."[illegible]hange the first paragraph to read as follows: "Phenobarbital Sodium conta[illegible]not less than 89 per cent and not more than 91.5 per cent of phenobarbital[illegible]$_{12}H_{12}N_2O_3$), calculated on a moisture-free basis, the moisture being deter[illegible]ed on a separate portion by drying at 140° C. for six hours. Insert: "*Sto*[illegible].—Preserve in tight containers." Under "Summarized Description" change[illegible]J.S.P., p. 284" in the last line of the second paragraph to read: "U.S.P. X[illegible]pp. 356–357."

Pilulæ Aloes et Mastic[illegible]—Page 341: The Second Supplement to N.F. VII permits, until further notice the omission of rose from this formula due to a shortage because of the war.

Pilulæ Cascaræ Compositæ—Page 341: Delete Strychnine Sulfate from the formula appearing in table headed "Pills of the National Formulary." The First Supplement to N.F. VI permits until further notice the substitution of 1 Gm. of Extract of Stramonium for the 0.8 Gm. of Extract of Belladonna called for.

Pilulæ Ferri Iodidi—Page 341: In the first line of the monograph cross out "Blancard's Pills" as a synonym for Pills of Ferrous Iodide. See N.F. VII, p. 330.

Pilulæ Hydrargyri Chloridi Mitis Compositæ—Pages 340 and 341: The First Supplement to N.F. VII permits the omission of Gamboge from the formula until further notice.

Pinus Alba—White Pine: This is not mentioned in "Principles of Pharmacy." It is official in N.F. VII and is dried inner bark of *Pinus Strobus*. It contains a volatile oil and is used in the preparation of cough syrups. Its dose is 2 Gm. (30 grains).

Pituitarium Anterior—Page 965: Change title to "Pituitarium Anterius."

Pituitarium Posterius—Page 964: Add to first paragraph: "The potency of Posterior Pituitary shall be such that 1 mg. shall possess an activity equivalent to not less than 1 U.S.P. Posterior Pituitary Unit. (The potency of 0.5 mg. of the U.S.P. Posterior Pituitary Reference Standard represents 1 U.S.P. unit.)" Change "Storage" to "Preserve in well-closed containers, preferably at a temperature not above 30° C." Change U.S.P. page reference to "U.S.P. XII, p. 365."

Plantaginis Semen—Page 709: Add another source: "*Plantago indica* Linné (*Plantago arenaria* Waldstein et Kitaibel), known in commerce as Spanish or French Psyllium Seed." See Second Supplement to N.F. VII.

Podophyllum—Page 879: In line three, change "4" to "5" and in line four, change "3" to "2." This monograph now appears in N.F. VII (pp. 337–338).

Populi Gemma—Poplar Bud: This does not appear in "Principles of Pharmacy." It is official in N.F. VII and is the air-dried, closed, winter leaf bud of *Populus candicans* Aiton, known in commerce as Balm of Gilead Buds, or of *Populus Tacamahacca* Miller (*Populus balsamifera* Linné), known in commerce as Balsam Poplar Buds (Fam. *Salicaceæ*). These leaf buds contain a volatile oil and are used as a stimulant and expectorant in cough preparations. The dose is 4 Gm. (60 grains). See N.F. VII, pp. 338–339 and Second Supplement to N.F. VII.

Potassii Bromidum—Page 465: In first line, change "100°" to "110°." Correct solubilities to "in 250 parts of alcohol, and in 5 parts of glycerin." Change U.S.P. page references to "U.S.P. XII, pp. 371–372."

Potassii Carbonas—Page 466: Delete second sentence of first paragraph. Change U.S.P. references to pp. 372–373.

Potassii Citras—Page 468: In first sentence change "150° C." to "180° C." Delete second sentence. Change U.S.P. references to p. 374.

Potassii et Sodii Tartras—Page 469: Delete second sentence of first paragraph. Change U.S.P. page references to "U.S.P. XII, pp. 375–376."

Potassii Iodidum—Page 470: In first line, change "100°" to "110°." Correct alcohol solubility to "soluble in 22 parts of alcohol" and add "soluble in 2 parts of glycerin and in 0.5 parts of boiling water." Change U.S.P. page references to "U.S.P. XII, pp. 377–378."

Potassii Nitras—Page 471: In first line change "when dried to constant weight at 100° C." to "when dried for 4 hours at 110° C." Change "Dose" to "1 Gm. (15 gr.)." Change U.S.P. page references to "U.S.P. XII, p. 378."

Pulsatilla—Pulsatilla (Pasqueflower): This is not mentioned in "Principles of Pharmacy." It is official in N.F. VII and is the dried herb of *Anemone pulsatilla, Anemone pratensis,* or *Anemone patens.* In contains a volatile oil and is used in doses of 0.3 Gm. (5 grains) in the treatment of amenorrhea and dysmenorrhea.

Pulveres Effervescentes Compositi—Page 314: Change "Dose" to read "The contents of a white and of a blue paper, each dissolved in about 2 fluidounces of water, the solutions mixed, and administered just after the effervescence begins to subside." Change U.S.P. page references to "U.S.P. XII, pp. 381–382."

Pulvis Sennæ Compositus—Page 316: This article now appears in N.F. VII. Under "Condensed Recipe" add "Note: Three per cent of the sucrose may be replaced by powdered starch. Do not dispense if the powder becomes hard and compact." For details, see N.F. VII, p. 348.

Quinidinæ Sulfas—Page 920: Change first sentence to "The sulfate of an alkaloid obtained from the bark of the stem or of the root of various species of *Cinchona* and their hybrids (Fam. *Rubiaceæ*)." Correct solubilities to "soluble in 100 parts of water, and in about 10 parts of alcohol." Add "soluble in 15 parts of boiling water." Change U.S.P. page references to "U.S.P. XII, pp. 384–385."

Quininæ Æthylcarbonas—Page 918: Add definition: "The ethylcarbonate of an alkaloid obtained from cinchona." Insert dose of "1 Gm. (15 grains)." Correct solubilities to "soluble in 3 parts of alcohol, in about 1 part of chloroform, and in 10 parts of ether." Change U.S.P. page references to "U.S.P. XII, pp. 385–386.'

Quininæ Bisulfas—Page 919: Add definition: "The bisulfate of an alkaloid obtained from cinchona." Insert dose of "1 Gm. (15 grains)." Change "Summarized Description" to read "White or colorless crystals, usually needle-like, or white, crystalline powder; odorless; very bitter taste; turns yellow on exposure to light; effloresces on exposure to dry air; soluble in 10 parts of water; in 25 parts of alcohol, in about 15 parts of glycerin, and in about 625 parts of chloroform; soluble in 1 part of boiling water and in 1 part of boiling alcohol." Change U.S.P. page references to "U.S.P. XII, pp. 386–387."

Quininæ Dihydrochloridum—Page 919: Add definition: "The dihydrochloride of an alkaloid obtained from cinchona." Insert dose of "1 Gm. (15 grains)." Change U.S.P. page references to "U.S.P. XII, pp. 387–388."

Quininæ et Ureæ Hydrochloridum—Page 919: Add, following first sentence: "It is a double salt of quinine and urea hydrochlorides." Correct solubilities to "soluble in 1 part of water and in 3 parts of alcohol." Dose does not appear in U.S.P. XII. Change U.S.P. page references to "U.S.P. XII, pp. 388–389."

Quininæ Sulfas—Page 920: Add definition: "The sulfate of an alkaloid obtained from cinchona." Correct alcohol solubility to "in about 120 parts of alcohol." Add "soluble in 35 parts of water at 100° C. and in about 10 parts of alcohol at 80° C." Insert dose of "0.6 Gm. (10 grains)." Change U.S.P. page references to "U.S.P. XII, pp. 390–391."

Residuum Ovarium—Page 967: Change title to "Residuum Ovarii."

Rubrum Scarlatinum—Page 781: Change "tolyl-azo-betanaphthol" to "o-tolyl azo-o-tolyl azo-β-naphthol."

Sabal—Page 852: Change title to "Serenoa." In first line, change "fruit of *Serenoa serrulata*" to "partially dried, ripe fruit of *Serenoa repens.*"

Saccharinum—Page 798: Definition does not appear in U.S.P. XII. Correct alcohol solubility to "and in 31 parts of alcohol" and add "soluble in about 25 parts of boiling water." Dose does not appear in U.S.P. XII. Add "Note—A 60 mg. portion of Saccharin is equivalent as a sweetening agent to approximately 30 Gm. of sucrose." Change U.S.P. page references to "U.S.P. XII, pp. 394–395."

Saccharinum Solubile—Page 799: Change title to "Saccharinum Sodicum—Saccharin Sodium." Definition does not appear in U.S.P. XII. Correct solubilities to "soluble in 1.5 parts of water and in about 50 parts of alcohol." Add "Note—A 60 mg. portion of Saccharin Sodium is equivalent in sweetening power to approximately 30 Gm. of sucrose." Change U.S.P. page reference to "U.S.P. XII, pp. 395–396."

Santalum Album—White Sandalwood: This is not mentioned in "Principles of Pharmacy." It is official in N.F. VII and is the heartwood of *Santalum album*. Each 100 Gm. of White Sandalwood yields not less than 3.5 cc. of volatile oil (Oil of Santal). The dose is 4 Gm. (60 grains).

Sapo Mollis—Page 743: Change title to "Sapo Mollis Medicinalis—Medicinal Soft Soap." Add definition: "Medicinal Soft Soap is a potassium soap made by the saponification of vegetable oils, excluding coconut oil and palm kernel oil, without the removal of glycerin.

"Soft Soap may be prepared extemporaneously in the following manner (Substitute for "Condensed Recipe" in "Principles of Pharmacy"): Mix 380 Gm. of the vegetable oil with 20 Gm. of oleic acid and heat to 80° C. Dissolve 91.7 Gm. of potassium hydroxide in a mixture of 50 cc. of glycerin and 100 cc. of distilled water, and add to hot oil mixture. Finally enough distilled water is added to make 1000 cc. For details of manufacture, see U.S.P. XII, p. 398.

"*Note.*—The vegetable oil may be corn, cottonseed, linseed, olive, soya bean, or similar oils which have a saponification value not greater than 205, and an iodine value not less than 80. The glycerin may be omitted."

Change "Summarized Description" to "Soft, unctuous, yellowish white to brownish or greenish yellow, transparent to translucent mass; slight, characteristic odor; alkaline taste; alkaline to indicators."

Add "*Storage*—Preserve in well-closed containers."

Change U.S.P. page references to "U.S.P. XII, pp. 398–399."

Sarsaparilla—Page 722: Change source to read: "Sarsaparilla is the dried root of *Smilax aristolochiæfolia* Miller, known in commerce as Mexican Sarsaparilla; or of *Smilax Regelii* Killip and Morton, known in commerce as Honduras Sarsaparilla; or of undetermined species of *Smilax*, respectively known in commerce as Ecuadorian and Central American Sarsaparilla (Fam. *Liliaceæ*)." Change U.S.P. page references to "U.S.P. XII, pp. 400–401."

Sassafras—Page 844: Change "*Sassafras variifolium*" to "*Sassafras albidum* (Nuttall) (Fam. *Lauraceæ*)." Add "It yields not less than 4.0 cc. of oil of sassafras from each 100 Gm. of drug."

Scilla—Page 718: In third line, delete "Squill" and insert "or Mediterranean Squill, or of *Urginea indica* Kunth, known in commerce as Indian Squill (Fam. *Liliaceæ*)." Change the U.S.P. page references to "N.F. VII, pp. 371–372." The dose does not appear in N.F. VII.

Serum Antimeningococcicum—Page 980: In first sentence, delete "of the genus *Equus*." Add the following statement: "It complies with the requirements of the National Institute of Health of the United States Public Health Service." For regulations and other details, see U.S.P. XII, p. 403.

Serum Antipneumococcicum—Page 981: Change the title and first paragraph to read as follows: "Serum Antipneumococcicum—Antipneumococcic Serum—Type Specific (Serum Antipneumococ.—Antipneumococcus Serum, Pneumonia Serum).

Antipneumococcic Serum is obtained from the blood of an animal which has been immunized with cultures of a pneumococcus (*Diplococcus pneumoniæ*) of one of the types for which a serum has been prepared and which has been standardized or is released by the National Institute of Health of the United States Public Health Service, and complies with the requirements of that agency of the Government.

Under "Summarized Description" in the first line of the first paragraph eliminate "type I" and insert "opalescent" after "clear." Change "Administration and Dosage" to read: "Dose.—Parenteral therapeutic, from 20,000 to 100,000 units" and add "Caution—Type XIV Antipneumococcic Serum produced by immunization of the horse shall not be administered to persons of blood group 'A.'"

Add the following: "*Regulations.*—The potency of Antipneumococcic Serum shall be expressed in units of protective antibody, and the unit shall be that established by the National Institute of Health of the United States Public Health Service.

The outside label must bear the name *Antipneumococcic Serum,* the specific type or types of pneumococcus represented, the minimum number of units in the package, the genus of animal employed, the manufacturer's lot number of the Serum, the name, address, and license number of the manufacturer, and a statement of the date beyond which the Serum may not be expected to retain the potency described by governmental authority."

Pneumonia mortality has been greatly reduced since these sera were made available. The title Serum Antipneumococcicum-I has been deleted as a synonym from the U.S.P. XII.

For further information, see U.S.P. XII, pp. 403–404.

Sodii Acetas—Page 480: Change "Storage" to "Preserve in tight containers." Change "Dose" to "1.5 Gm. (22 grains)." Change U.S.P. page references to "N.F. VII, p. 375."

Sodii Bicarbonas—Page 486: In first line, change "to constant weight over sulfuric acid" to "over sulfuric acid for 6 hours." See U.S.P. XII, pp. 408–409. Change "Dose" to 2 Gm. (30 gr.).

Sodii Biphosphas—Page 491: Delete water content from rubric (second sentence). Change "Storage" to "Preserve in well-closed containers." Change U.S.P. page references to "U.S.P. XII, pp. 409–410."

Sodii Bromidum—Page 482: In first line, change "to constant weight at 100° C." to "at 110° C. for 6 hours." Change "Storage" to "Preserve in tight containers." Change U.S.P. page references to U.S.P. XII, p. 411."

Sodii Carbonas Monohydratus—Page 483: Change the first paragraph to read as follows: "Monohydrated Sodium Carbonate, when dried to constant weight at 110° C., contains not less than 99 5 per cent of Na_2CO_3." Change U.S.P. references to "pp. 412–413."

Sodii Citras—Page 487: In first line, change "when rendered anhydrous by drying at 150° C." to "when dried to constant weight at 150° C." Delete second sentence. Change "Storage" to "Preserve in tight containers." Change U.S.P. page references to "U.S.P. XII, pp. 414–415."

Sodii Iodidum—Page 487: Deete water content from rubric (second sentence). Change "Storage" to "Preserve in tight containers." Change U.S.P. page references to "U.S.P. XII, p. 416."

Sodii Nitris—Page 488: Change first sentence to: "Sodium Nitrite, when dried over sulfuric acid for 18 hours, contains not less than 97 per cent of $NaNO_2$." Change "Storage" to "Preserve in tight containers." In first line of "Summarized Description," delete "colorless hexagonal crystals or" and substitute "or white to slightly yellow." Change U.S.P. page references to "U.S.P. XII, p. 417."

Sodii Phosphas—Page 488: Delete water content from rubric (second sentence). Change "Storage" to "Preserve in tight containers." In second line, on page 489, delete "monoclinic prisms or" and substitute "or white." Change U.S.P. page references to "U.S.P. XII, pp. 418–419."

Sodii Salicylas—Page 491: In first line, change "to constant weight at 100° C." to "at 110° C. for 4 hours." Change "Storage" to "Preserve in well-closed, light-resistant containers." Correct solubilities to "soluble in 1 part of water and in 10 parts of alcohol" and add "soluble in about 4 parts of glycerin." Change "Dose" to "0.3 Gm. (5 grains)" and change U.S.P. page references to "U.S.P. XII, pp. 420–421."

Sodii Sulfas—Page 492: In first line, change "rendered anhydrous by drying at 120° C." to "dried to constant weight at 110° C." Delete second sentence. Change "Storage" to "Preserve in tight containers, preferably at a temperature not above 30° C." Change U.S.P. page references to "U.S.P. XII, p. 422."

Sodii Thiosulfas—Page 493: In first line, change "rendered anhydrous by drying to constant weight at 100° C." to "when dried to constant weight at 100° C." and delete second sentence. Change "Storage" to "Preserve in tight, light-resistant containers." Insert before the dose "Oral or intravenous," and change U.S.P. page references to "U.S.P. XII, pp. 423–424."

Spiritus Ætheris—Page 205: Change the word "ether" in the first line of the monograph to "ethyl oxide."
Page 206: In the table of Spirits of the National Formulary in the column headed "Ingredients," change the word "ether" to "ethyl oxide."

Spiritus Ætheris Compositus—Page 205: Change the word "ether" in the second line of the monograph to "ethyl oxide."
Page 206: In the table of Spirits of the National Formulary in the column headed "Ingredients," change the word "ether" to "ethyl oxide."

Spiritus Ammoniæ Aromaticus—Page 506: In first line figure should be "1.7." Change "Storage" to read: "Preserve in tight, light-resistant containers, preferably at a temperature not above 30° C." Due to shortages of stocks of volatile oils both the oil of lavender and oil of myristica may be omitted from the formula as directed by sheet supplements issued subsequent to the publication of U.S.P. XII. This change is to remain in force until rescinded by official action. Change U.S.P. page references to "U.S.P. XII, pp. 424–425."

Spiritus Camphoræ—Page 203: Change the first paragraph to read as follows: "Spirit of Camphor is an alcoholic solution containing, in each 100 cc., not less than 9.2 Gm. and not more than 10.4 Gm. of camphor, at 25° C." Change references to U.S.P. to pages 426–427.

Stomachus—Page 966: Change title to "Stomachus Pulveratus—Powdered Stomach." In second line, delete "that antianemia factor" and insert "factors." Delete last sentence and insert in its place: "The activity is readily destroyed when the preparation is suspended in a hot liquid The approximate anti-anemic potency of Powdered Stomach in pernicious anemia is expressed in U.S.P. Units and conforms to all other provisions outlined under *Anti-anemia Preparations,* U.S.P. XII, page 553." Change "Dose" to "One U.S.P. Unit daily." See U.S.P. XII, p. 432.

Stramonium—Page 938: Change the second paragraph to read: "Stramonium yields not less than 0.25 per cent of the alkaloids of Stramonium," etc. Change page reference to U.S.P. to p. 433. The dose does not appear in U.S.P. XII.

Strophanthinum—Page 717: In first sentence, change "glucoside" to "glycoside" and "glucosides" to "glycosides." Delete balance of second sentence, after word "potency," and substitute "per mg. equivalent to 0.5 mg. of U.S.P. Ouabain Reference Standard, U.S.P. XII, page 607." Before the dose, insert "Intravenous" and change the U.S.P. page references to "U.S.P XII, p. 434."

Syrupus Acidi Hydriodici—Page 444: Under "Condensed Recipe" change "130 cc. of diluted hydriodic acid" in the first line to "140 cc. of diluted hydriodic acid." See U.S.P. XII, pp. 450–451.

Syrupus Ammonii Hypophosphitis—Page 223: The Second Supplement to N.F. VII permits, until further notice, a reduction in the quantity of glycerin in this formula from 300 cc. to 50 cc., and the replacement of the 250 Gm. of dextrose by enough syrup to make 1000 cc. The amount of distilled water is reduced to 100 cc. For revised formula and directions for preparation, see Second Supplement to N.F. VII. The N.F. VII formula had been previously changed from that appearing in "Principles of Pharmacy" in that dextrose was substituted for the syrup in the N.F. VI formula.

Syrupus Bromidorum—Page 223: The First Supplement to N.F. VII suggests the use of 16 cc. of Compound Solution of Amaranth (see Liquor Amaranthi Compositus in this supplement) in place of the Compound Tincture of Cudbear.

Syrupus Cacao Præparati—Page 223: Change Latin title to "Syrupus Cacao" and change English title to "Syrup of Cacao." Change ingredients, in third column of table, to "Cacao; sucrose; gelatin; distilled water. Tincture of vanilla as flavor."

Syrupus Calcii Lactophosphatis—Page 677: The Second Supplement to N.F. VII permits, until further notice, a reduction in the quantity of glycerin in this formula from 300 cc. to 50 cc., and the replacement of the 250 Gm. of dextrose by 650 Gm. of sucrose. The First Supplement to N.F. VII had previously permitted the substitution of water in place of the 50 cc. of orange flower water. For revised formula and directions for preparation, see Second Supplement to N.F. VII. A statement has also been added to "Storage" advising that this syrup should not be dispensed if darkened in color. The N.F VII formula had been changed but this revised formula is the same as the N.F. VI formula with the exception of the orange flower water. In the first line on page 678 insert after "agitation" "Now add 50 cc. of glycerin "

Syrupus Cinnamomi—Page 223: The First Supplement to N.F VII suggests the use of 60 cc. of Compound Solution of Amaranth (see Liquor Amaranthi Compositus in this supplement) in place of the Compound Tincture of Cudbear.

Syrupus Ferri Iodidi—Page 562: This syrup is now official in N.F. VII. In the fifth line of the paragraph headed "Remarks," at the end of the sentence, insert the following: "For the purpose of retarding discoloration, 1.3 Gm. of citric acid may replace the hypophosphorous acid in the formula." See N.F. VII, pp. 406–407.

Syrupus Hypophosphitum—Page 222: The Second Supplement to N.F. VII permits, until further notice, a reduction in the quantity of glycerin in this formula from 300 cc. to 50 cc., and the replacement of the 250 Gm. of dextrose by 600 Gm. of sucrose. For revised formula and directions for preparation, see Second Supplement to N.F. VII. A statement has also been added to "Storage" advising that this syrup should not be dispensed if brownish in color. The N.F. VII formula had been changed but this revised formula is the same as the N.F. VI formula.

Syrupus Hypophosphitum Compositus—Page 222: The First Supplement to N.F. VII permits the omission of the quinine from the formula until further notice. The Second Supplement permits, until further notice, the use of a formula in which the glycerin is reduced from 300 cc. to 50 cc., and 700 Gm. of sucrose is substituted for the 250 Gm. of dextrose. For revised formula and directions for preparation, see Second Supplement to N.F. VII. A statement has also been added to "Storage" advising that the syrup should not be dispensed if brownish in color.

Syrupus Ipecacuanhæ—Page 219: Change "Dose" to "Emetic, 8 cc. (2 fluidrachms)." Change U.S.P. page references to "U.S.P. XII, pp. 453–454."

Syrupus Pini Albæ Compositus—Pages 222–223: The First Supplement to N.F. VII suggests the use of 7 cc. of a 5 per cent solution of Amaranth in place of the Cudbear. The Second Supplement permits, until further notice, the omission of the glycerin and increases the quantity of sucrose to 700 Gm.

Syrupus Pruni Virginianæ—Page 220: Although the formula and procedure appearing in U.S.P. XII have been changed, the First U.S.P. Sheet Supplement directs the return to the U.S.P. XI formula to conserve glycerin so the information appearing in Principles of Pharmacy is substantially correct.

Taraxacum—Page 879: In first and second lines, change *"Leontodon Taraxacum"* to *"Taraxacum officinale* or *Taraxacum lævigatum."*

Theophyllina cum Æthylenediamina—Page 763: Change title to "Theophyllina Æthylenediaminica—Theophylline Ethylenediamine." Change the first paragraph to read as follows: "Theophylline Ethylenediamine contains not less than 75 per cent and not more than 82 per cent of anhydrous theophylline ($C_7H_8N_4O_2$), and not less than 12.3 per cent and not more than 13.8 per cent of ethylenediamine [$C_2H_4(NH_2)_2$]." Under "Summarized Description" in the second line add "Aqueous solution may become turbid on standing." Change dose to 0.2 Gm. (3 gr.). Change "U.S.P., p. 384" at the end of the second paragraph to read: "U.S.P. XII, pp. 498–499.

Theophyllina cum Sodii Acetate—Page 762: Change to "Theophyllina et Sodii Acetas." In first sentence, change "contains" to "yields" and add sentence: "It is a hydrated mixture of theophylline sodium ($C_7H_7N_4O_2Na$) and sodium acetate ($NaC_2H_3O_2$) in approximately molecular proportion." Change U.S.P. page references to "U.S.P. XII, p. 499."

Thymol—Page 821: Change "Dose" to "Anthelmintic, divided into three doses, 2 Gm. (30 grains)." Change U.S.P. page references to "U S.P. XII, pp. 501–502."

Thymus—Thyme (Common Thyme or Garden Thyme): This is not mentioned in "Principles of Pharmacy." It is official in N.F. VII and consists of the dried leaves and flowering tops of *Thymus vulgaris*. It yields not less than 1.5 cc. of volatile oil of Thyme from each 100 Gm. The dose is 4 Gm. (60 grains).

Tinctura Aconiti—Page 243: This article is now official in N.F. VII. Under "Condensed Recipe" change second sentence to read as follows: "Immediately add sufficient hydrochloric acid to this percolate to produce a *p*H of 3 ± 0.2. Assay a portion of the percolate, and adjust the volume of the remaining liquid by dilution with the menstruum, including sufficient hydrochloric acid to produce a *p*H of 3 ± 0 2, so that the finished Tincture will conform to the biological standard." For *details* and *assay*, see N. F. VII, pp. 440–441.

Tinctura Cannabis—Pages 252 and 255: Deleted from N.F. VI as of January 1, 1939 and does not appear in N.F. VII.

Tinctura Digitalis—Page 247: In second line, delete balance of sentence after word "shall" and substitute: "be equivalent to 1.0 U.S.P. Digitalis Unit." Add "Note—The attention of Physicians is called to the fact that U.S.P. XII Tincture of Digitalis is materially reduced in potency when compared with the U.S.P. XI Tincture." Change "Alcohol Content" to "70 to 75 per cent by volume" and change U.S P. page references to "U.S.P. XII, pp 509–511."

Tinctura Ferri Chloridi—Page 566: This article now official in N.F. VII. After the second paragraph insert "*Alcohol Content*—From 58 to 64 per cent, by volume, of C_2H_5OH." See N F. VII, p. 451.

Tinctura Ferri Citrochloridi—Page 255: In the table of Tinctures of the National Formulary, in the column headed "English name or synonym," cross out "Tasteless tincture of iron."

Page 567: At the end of the first sentence of the monograph insert: "The synonyms, *tasteless tincture of iron* and *tasteless tincture of ferric chloride* were deleted from N.F. VI as of January 1, 1939," and do not appear in N.F. VII.

Tinctura Gambir Composita—Page 253: In the third line of the monograph before the word "with" insert "for 24 hours." In the fourth line of the monograph before the word "to" insert "and percolate slowly." See N.F. VII, p. 452.

Tinctura Hyoscyami—Page 248: Under "Remarks" change the second sentence to read: "The alkaloid content is determined by a method described in the U.S.P. XII, pp. 511–512."

Tinctura Iodi—Page 427: In second line of definition change "6.5" to "6.8." After the paragraph headed "Storage," insert the following: "*Summarized Description.* Reddish-brown, transparent liquid having the odor of alcohol and iodine."

"*Alcohol Content.*—83 to 88 per cent, by volume, of C_2H_5OH."

For tests for *identity* see U.S.P. XII, p. 512. Under "Assay" change "U.S.P., p. 401" to read: "U.S.P. XII, p. 512."

Tinctura Iodi Mitis—Page 248: In second line, change "2.5" to "2.6." Change "Storage" to "Preserve in tight containers." In fifth line, change "48" to "50" and under "Condensed Recipe," change "sodium iodide, 23 Gm." to "sodium iodide, 24 Gm." Change U.S.P. page references to "U.S.P. XII, p. 513."

Tinctura Nucis Vomicæ—Page 250: The first line should read as follows: "Tinctura of Nux Vomica yields, from each 100 cc., not less than 0.105 Gm. and not more than 0.125 Gm. of strychnine." In line two under "Condensed Recipe" change "alcohol, 50 cc." to "alcohol, 150 cc." In line four change "0.75 cc." to "0.8 cc." and "24.25 cc." to "24.2 cc."; in fifth line delete rest of sentence after word "cc." and add "distilled water to make each 100 cc. contain 0.115 Gm. of strychnine. Keep the Tincture at a temperature of 5° C. for 30 minutes, and filter."

Tinctura Opii Camphorata—Page 251: Under "Condensed Recipe" insert: "The following alternative method of preparation may be used: Macerate 4.3 Gm. of powdered opium, 3.8 Gm. benzoic acid, 3.8 Gm. camphor and 3.8 cc. oil of anise for five days, with occasional agitation, in a mixture of 38 cc. of glycerin and 900 cc. of diluted alcohol. Filter and make up to 950 cc. with diluted alcohol. Assay and dilute with sufficient diluted alcohol containing in each 100 cc., 0.4 cc. oil of anise, 0.4 Gm. benzoic acid, 0.4 Gm. camphor and 4 cc. glycerin, to produce a Tincture of official morphine strength." For details, see U.S.P. XII, pp. 516–517.

Tinctura Persionis Composita—Page 256: The First Supplement to N.F. VII suggests the use of 35 cc. of a 5 per cent solution of Amaranth in place of the Tincture of Cudbear. See *Liquor Amaranthi Compositus*.

Tinctura Stramonii—Page 251: The first paragraph should be changed to read: "Tincture of Stramonium yields, from each 100 cc., not less than 0.022 Gm. and not more than 0.028 Gm. of the alkaloids of Stramonium." See U.S.P. XII, p. 518.

Page 252: Under "Remarks," add "For assay, see U.S.P. XII, p. 518."

Tinctures—Page 239: For additional information, see new material under "Tincturæ" on pages 505 and 506 of U.S.P. XII, and on pages 439 and 440 of N.F. VII.

Toxinum Diphthericum Detoxicatum—Page 981: Change Latin title to "Toxoidum Diphthericum." Strike out the last two sentences of the first paragraph and insert the following: "Diphtheria Toxoid complies with the requirements of the National Institute of Health of the United States Public Health Service. A concentrated Diphtheria Toxoid may be produced in the following form known as:

"DIPHTHERIA TOXOID, Alum Precipitated

"Refined Diphtheria Toxoid

"This is a turbid, white, slightly gray, or slightly pink suspension prepared by adding a sterile aqueous solution of alum to Diphtheria Toxoid, washing the resultant precipitate with isotonic solution of sodium chloride, and resuspending it in isotonic solution of sodium chloride to which a suitable preservative may be added.

"Alum Precipitated Diphtheria Toxoid shall be labeled as is required for Diphtheria Toxoid with the additional designation *Alum Precipitated* on the labels of the finished package.

"It shall meet the requirements as given under Diphtheria Toxoid with the exception of the requirement for antigenicity. It shall also meet the following requirements:

"The dose of Alum Precipitated Diphtheria Toxoid for the adult human, when administered subcutaneously to a guinea pig weighing 500 Gm. shall produce at least two units of antitoxin per cc. of blood serum at the end of four weeks. At least four guinea pigs shall be used for this test, but the blood serum from all of the test animals may be pooled for the test for antitoxic content.

"The finished product shall contain not more than 20 mg. of alum per cc., the calculation being based on the total amount of alum added for precipitation."

Change "Dose" to read: "Hypodermic, for active immunization, 1 cc., to be repeated at proper intervals until a negative Schick test is obtained."

For further details and regulations, see U.S.P. XII, pp. 523–524.

Toxinum Diphthericum Diagnosticum—Page 982: In the first line, insert word "sterile" before "solution." Add after first sentence: "Diphtheria Toxin for the Schick Test complies with the requirements of the National Institute of Health of the United States Public Health Service." For revised description and regulations, see U.S.P. XII, pp. 520–521.

Toxinum Scarlatinæ Streptococcicum—Page 982: Substitute for the first paragraph: "Scarlet Fever Streptococcus Toxin is a sterile solution in a medium containing not more than 1 per cent of peptone but no meat extractive, of certain products including a soluble toxin, resulting from the growth in the broth of suitable strains of hemolytic streptococci (*Streptococcus scarlatinæ*). Scarlet Fever Streptococcus Toxin complies with the requirements of the National Institute of Health of the United States Public Health Service." Change "Summarized Description" to "Transparent liquid having color of the medium in which it is made; slight odor which is altered somewhat by preservative used." Change "Dose" to "Diagnostic, for determining susceptibility (Dick test), 0.1 cc. of the dilution, representing one-fiftieth of the minimum lethal dose." For regulations and other details, see U.S P. XII, pp. 520–521.

Toxitabellæ Hydrargyri Bichloridi Magnæ—Page 347: The first paragraph should read as follows: "Large Poison Tablets of Mercury Bichloride contain an average of not less than 0.42 Gm. and not more than 0.52 Gm. of $HgCl_2$, with a sufficient quantity of a suitable excipient or diluent." See U.S.P. XII, p. 522. Add "Note—One Large Poison Tablet of Mercury Bichloride added to 475 cc. (1 pint) of water makes a '1 to 1000' solution"

Toxitabellæ Hydrargyri Bichloridi Parvæ—Page 349: In the second line, change "0.1125" to "0 11" and "0.1375" to "0.14." Add "Note—One Small Poison Tablet of Mercury Bichloride added to 120 cc. (4 fluidounces) of water makes a '1 to 1000 solution.'" Change U S.P. page references to "U.S P. XII, p. 523."

Tryparsamidum—Page 785: Add to first paragraph: "Tryparsamide must be prepared in an establishment licensed for the purpose by the United States Government upon recommendation of the Surgeon General of the United States Public Health Service Each lot of the product before being offered for sale must comply with the toxicity, labeling, and other requirements of the National Institute of Health and be released by the Institute." Change "Storage" to "Preserve in tight containers, preferably at a temperature not above 20° C." Insert before the dose "Caution. Intravenous." Requirements for labeling now appear in U.S.P. XII. Change U S.P page references to "U.S.P. XII, pp. 530–531."

Tuberculinum Pristinum—Page 983: After the first sentence, add: "Old Tuberculin complies with the requirements of the National Institute of Health of the United States Public Health Service." Change "Dose" to "Diagnostic, intracutaneous—0.000,01 cc. to 0.001 cc.; therapeutic, subcutaneous—0.000,000,01 cc. to 0.000,001 cc" See U S.P. XII, pp. 531–532.

Unguentum—Page 363: Change title to "Unguentum Album—White Ointment." In line 2 of Condensed Recipe change "U.S.P., p. 415" to "U.S.P. XII, p. 533."

Unguentum Acidi Borici—Page 365: Substitute for Condensed Recipe: "Levigate 10 Gm. Boric Acid with 5 Gm. Wool Fat to smooth paste and mix with 85 Gm. White Ointment." (See Unguentum above.) "For details and assay, see U.S.P. XII, p. 532."

Unguentum Acidi Tannici—Page 365: Substitute for Condensed Recipe: "Dissolve 20 Gm. Tannic Acid and 0.2 Gm. Sodium Sulfite in 20 Gm. Glycerin using gentle heat, and mix with 59.8 Gm. Yellow Ointment." (See Unguentum Flavum, p. 47 of this supplement.) "For details, see U.S.P. XII, p. 533."

Unguentum Aquæ Rosæ—Pages 365–366: The U.S.P. formula calls for 2.5 cc. Rose Water, 7 cc. Distilled Water, and 0.01 cc. Oil of Rose in place of "Stronger Rose Water," 9.50 Gm. in the formula appearing in Principles of Pharmacy. The First U.S.P. XII Sheet Supplement permits the substitution of Persic Oil (see p. 32 of this supplement) for the Expressed Oil of Almond and Distilled Water for the Rose Water; the Oil of Rose may be omitted.

Unguentum Belladonnæ—Page 366: Substitute for first two lines and Condensed Recipe: "Belladonna Ointment yields not less than 0.110 per cent and not more than 0.140 per cent of the alkaloids of belladonna leaf.

Condensed Recipe.

Triturate 10 Gm. of Pilular Extract of Belladonna with 5 cc. of Diluted Alcohol until smooth and mix with 85 Gm. of Yellow Ointment." (See Unguentum Flavum, p. 47 of this supplement.) "For details and assay, see U.S.P. XII, pp. 534–535."

Unguentum Chrysarobini—Page 366: Substitute for Condensed Recipe: "Triturate 6 Gm. of Chrysarobin with 7 Gm. of Chloroform, and gradually add 87 Gm. of melted Yellow Ointment" (see Unguentum Flavum, p. 47 of this supplement) "and stir until congealed. For details see U.S.P. XII, p. 535."

Unguentum Hydrargyri Ammoniati—Pages 366–367: Substitute for first two lines and Condensed Recipe: "Ammoniated Mercury Ointment contains an amount of ammoniated Mercury corresponding to not less than 3.5 per cent and not more than 4.5 per cent of Hg.

Condensed Recipe.

Levigate 5 Gm. of Ammoniated Mercury, in very fine powder, with 5 Gm. of Wool Fat until smooth and mix with 90 Gm. of White Ointment." (See Unguentum, page 87.) "For details and assay, see U.S.P. XII, p. 536."

Unguentum Hydrargyri Forte—Page 367: Change first two lines to read: "Strong Mercurial Ointment contains not less than 47.5 per cent and not more than 52.5 per cent of Hg." Change in last line of Condensed Recipe "U.S.P., p. 420" to U.S.P. XII, pp. 536–537."

Unguentum Hydrargyri Mite—Page 367: Substitute for first two lines and *Condensed Recipe:* "Mild Mercurial Ointment contains not less than 9 per cent and not more than 11 per cent of Hg.

Condensed Recipe.

Mix 200 Gm. of Strong Mercurial Ointment with 800 Gm. of White Ointment." (See Unguentum, page 87.) "For details and assay, see U.S.P. XII, p. 537."

Unguentum Hydrargyri Oxidi Flavi—Page 368: In place of second line of Caution substitute "with metallic utensils or containers except when made of tin or when tin-coated." Substitute for Condensed Recipe: "Triturate 1 Gm. of Yellow Mercuric Oxide, in very fine powder, with 1 Gm. of Liquid Petrolatum until smooth and mix with 98 Gm. of Yellow Ointment." (See Unguentum Flavum, p. 47 this supplement.) "For details and assay, see U.S.P. XII, p. 538."

Unguentum Iodi—Page 368: In second line of caution change word "iron" to "metallic." Substitute for Condensed Recipe: "Dissolve 4 Gm. Iodine and 4 Gm. Potassium Iodide in 12 Gm. Glycerin, preferably in a glass mortar, and mix with 80 Gm. Yellow Ointment." (See Unguentum Flavum, p. 47 this supplement.) "For details and assay, see U.S.P. XII, pp. 538–539."

Unguentum Mentholis Compositum—Page 372: In the table of Ointments of the National Formulary, in the column headed "English name or synonym," cross out "Analgesic Balm." In the column headed "Ingredients," change "menthol, 15 Gm." to "menthol, 10 Gm."

Page 373: In the second line of the monograph change "(15 per cent)" to "(10 per cent)."

Unguentum Phenolis—Page 368: Change Condensed Recipe to: "Mix 2 Gm. Phenol with 98 Gm. Yellow Ointment." (See Unguentum Flavum, p. 47 this supplement.) "For details and assay, see U.S.P. XII, p. 539."

Unguentum Picis Pini—Page 369: Substitute for Condensed Recipe: "Mix 50 Gm. Pine Tar with 50 Gm. Yellow Ointment." (See Unguentum Flavum, p. 47 this supplement.) "For details, see U.S.P. XII, p. 540.

Unguentum Resorcinolis Compositum—Page 372: The First Supplement to N.F. VII permits until further notice the replacement of the Rectified Oil of Birch Tar by 2 Gm. of Juniper Tar and the increase of the Petrolatum from 25 Gm. to 29 Gm.

Unguentum Sulfuris—Page 369: Substitute for Condensed Recipe: "Levigate 15 Gm. Precipitated Sulfur with 7 Gm. Wool Fat and mix with 78 Gm. White Ointment." (See Unguentum, page 87.) "For details and assay, see U.S.P. XII, p. 540."

Unguentum Zinci Oxidi—Page 369: Substitute for first two lines and Condensed Recipe: "Zinc Oxide Ointment contains not less than 18.5 per cent and not more than 21.5 per cent of ZnO.

Condensed Recipe.

Levigate 20 Gm. of Zinc Oxide, in very fine powder, with 7 Gm. Wool Fat until smooth and mix with 73 Gm. White Ointment." (See Unguentum, page 87) "For details, see U.S.P. XII, p. 541"

Uva Ursi—Page 721: In the second line, after *"Uva-ursi"* insert "or its varieties *coactylis* and *adenotricha.*"

Vaccinum Rabies—Page 983: In the first line, change "a sterile" to "an uncontaminated" and in the second line, change "is contained in" to "is obtained from." In the third line, delete "or dead of" and add at the end of the paragraph: "Rabies Vaccine complies with the requirements of the National Institute of Health of the United States Public Health Service." The U.S.P. XII dose is: "Hypodermic, for active immunization, the contents of one container, to be repeated at proper intervals." For regulations and other details, see U.S.P. XII, p. 542.

Vaccinum Typho-Paratyphosum—Page 984: In the second line, change word "physiological" to "isotonic" and insert after word "chloride" the phrase "or other suitable diluent." In the first line on page 985, substitute for "(*Eberthella typhi*)" the phrase "(*Eberthella typhosa*), of a strain selected for high antigenic efficiency." In the fourth line, change "500,000,000" to "250,000,000" and add at the end of the paragraph: "This vaccine complies with the requirements of the National Institute of Health of the United States Public Health Service." Under "Potency" change "500,000,000" to "250,000,000 of each of the." For other details and regulations, see U.S.P. XII, pp. 543–544.

Vaccinum Typhosum—Page 984: In the second line, change "(*Eberthella typhi*)" to "(*Eberthella typhosa*), of a strain selected for high antigenic efficiency" and change word "physiological" to "isotonic." Add at end of the paragraph: "It complies with the requirements of the National Institute of Health of the United States Public Health Service." For further information and regulations, see U.S.P. XII, p. 543.

Vaccinum Variolæ—Page 985: In the second line, change "species" to "family." In the fourth line, change "maximum potency" to "suitable development" and in the sixth line, change "shall" to "must" and "bromcresol" to "bromocresol." Add at the end of the paragraph: "Smallpox Vaccine complies with the requirements of the National Institute of Health of the United States Public Health Service." Change "Summarized Description" to read as follows: "Grayish, turbid suspension; may have odor and trace of color due to preservative being present." For precautions, regulations and other details, see U.S.P. XII, pp. 544–545.

Valeriana—Page 844: This article is now official in N.F. VII. The First Supplement to N.F. VII directs the insertion of the following after the official definition: "Note—Until further notice, when Valerian is prescribed or demanded, Indian Valeriana from *Valeriana Wallichii*, D.C. may be dispensed or supplied." In the second paragraph of the monograph in "Principles of Pharmacy," change "5" to "4" and "10" to "8." See N.F. VII, pp. 478–479.

Vanilla—Page 805: Insert at end of the first line: "known in commerce as Mexican or Bourbon Vanilla, or of *Vanilla tahitensis* Moore, known in commerce as Tahiti Vanilla. Change U.S.P. page references to "U.S.P. XII, p. 545."

Viburnum Opulus—Page 844: Change synonym to "True Cramp Bark" and add another synonym "High-bush Cranberry Bark." In the second line, insert after "Aiton," "(*Viburnum trilobum* Marshall)." See N.F. VII, p. 481. The Second Supplement to N.F. VII changes the dose to "4 Gm. (60 grains)."

Viburnum Prunifolium—Page 844: In the first line, change "bark" to "dried bark of the root or stem" and add "*Viburnum rufidulum*" as another source. Change "Dose" to "4 Gm. (60 grains)." See N.F. VII, p. 482.

Zea—Zea (Corn-silk): This does not appear in "Principles of Pharmacy." It is official in N.F. VII and consists of the fresh styles and stigmas of *Zea Mays*. It is used as a diuretic in doses of 4 Gm. (60 grains). See N.F. VII, p. 484 and Second Supplement to N.F. VII.

Zinci Acetas—Page 535: In the first sentence, change "83.16" to "82.74" and "99.5" to "99." Correct solubilities to "soluble in 2.5 parts of water and in 30 parts of alcohol." Change "Storage" to "Preserve in tight containers" and change the U.S.P. page references to "U.S.P. XII, p. 546."

Zinci Sulfas—Page 538: In the first sentence,, change "55.86" to "55.58," "58.63" to "61.0" and "99.5" to "99." The dose does not appear in U.S.P. XII. Change the U.S.P. page references to "U.S P. XII, p. 549."

Zingiber—Page 856: In the first sentence, delete "with outer cortical layers removed" and add at end: "and African Ginger. The outer cortical layers are often either partially or completely removed." At the end of the second sentence add: "and not less than 12 per cent of cold-water extractive " Change N.F. VI page reference to "N.F. VII, p. 347." The monograph for ginger appears in U.S.P. XII on pages 549 and 550

INTERNATIONAL ATOMIC WEIGHTS 1941

Sym.	*At. Wt.*	*At. No.*	*Sym.*	*At. Wt.*	*At. No.*	*Sym.*	*At. Wt.*	*At. No.*	*Sym.*	*At. Wt.*	*At. No.*
A	39.944	18	Eu	152.0	63	N	14.008	7	Se	78.96	34
Ag	107.880	47	F	19.00	9	Na	22.997	11	Si	28.06	14
Al	26.97	13	Fe	55 85	26	Nd	144.27	60	Sm	150.43	62
As	74.91	33	Ga	69.72	31	Ne	20.183	10	Sn	118 70	50
Au	197.2	79	Gd	156 9	64	Ni	58.69	28	Sr	87.63	38
B	10.82	5	Ge	72.60	32	O	16 0000	8	Ta	180.88	73
Ba	137.36	56	H	1.0080	1	Os	190.2	76	Tb	159 2	65
Be	9.02	4	He	4.003	2	P	30.98	15	Te	127.61	52
Bi	209.00	83	Hf	178.6	72	Pa	231	91	Th	232.12	90
Br	79.916	35	Hg	200.61	80	Pb	207.21	82	Ti	47.90	22
C	12.010	6	Ho	164.94	67	Pd	106.7	46	Tl	204.39	81
Ca	40.08	20	I	126.92	53	Pr	140.92	59	Tm	169.4	69
Cb	92.91	41	In	114.76	49	Pt	195.23	78	U	238.07	92
Cd	112.41	48	Ir	193.1	77	Ra	226.05	88	V	50.95	23
Ce	140.13	58	K	39.096	19	Rb	85.48	37	W	183.92	74
Cl	35.457	17	Kr	83.7	36	Re	186.31	75	Xe	131.3	54
Co	58.94	27	La	138.92	57	Rh	102.91	45	Y	88 92	39
Cr	52.01	24	Li	6 940	3	Rn	222	86	Yb	173.04	70
Cs	132.91	55	Lu	174.99	71	Ru	101.7	44	Zn	65 38	30
Cu	63.57	29	Mg	24.32	12	S	32.06	16	Zr	91.22	40
Dy	162.46	66	Mn	54.93	25	Sb	121.76	51			
Er	167.2	68	Mo	95.95	42	Sc	45.10	21			

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